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PRIMARY SYSTEMATISED AMYLOIDOSIS WITH MACROGLOSSIA.

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PRIMARY systematized amyloidosis is a rare disease which differs markedly from secondary amyloidosis. From the work of Königstein (1925) and of Lubarsch (1929) we recognize this striking clinical picture and accept certain diagnostic criteria :

(i) There is no chronic suppuration, granulomatous disease or rheumatoid arthritis, as is the case in secondary amyloidosis.

(ii) The distribution of amyloid is distinctive, with widespread involvement of muscle and small blood-vessels. Particular features are amyloid macroglossia, gastro-intestinal and cutaneous infiltration, and heart failure.

(iii) Metachromatic staining for this kind of amyloid is variable.

The association of amyloidosis with myelomatosis is of particular interest, as the amyloidosis may be of the " primary " type. Weber (1903) was the first to describe this : a case of myelomatosis with Bence-Jones proteinuria and amyloid infiltration of the tongue, though the condition may not be acceptable as " primary " in the presence of some gummata. His further publications have drawn attention to systematized amyloidosis with macroglossia accompanying plasma-cell myeloma (Weber *et al.*, 1937 ; Stewart and Weber, 1938). Pick (1931) emphasized the predilection for tongue involvement in atypical amyloidosis of skin and muscle.

Four cases of this syndrome were recorded by Brunsting and Macdonald (1947) with plasma-cell myeloma in three of them. Our case is a further example of this kind.

Case Report.

Mrs. E. H—, aged 50, was admitted to hospital on 3 June 1950 with skin lesions, enlarged tongue, weakness and early cardiac failure.

She had had symptoms of angina pectoris for two years before admission to hospital, having previously had no serious illness. Nine months before admission she noticed tenderness of the hands with cracking at the flexures of the fingers. There followed soreness at the corners of the mouth, and little lumps or " blisters " appeared there and on the eyelids and ears. At the same time her tongue became painful and swollen. For the few months before admission she complained of progressive weakness and tiredness, and she was able to walk only a short distance

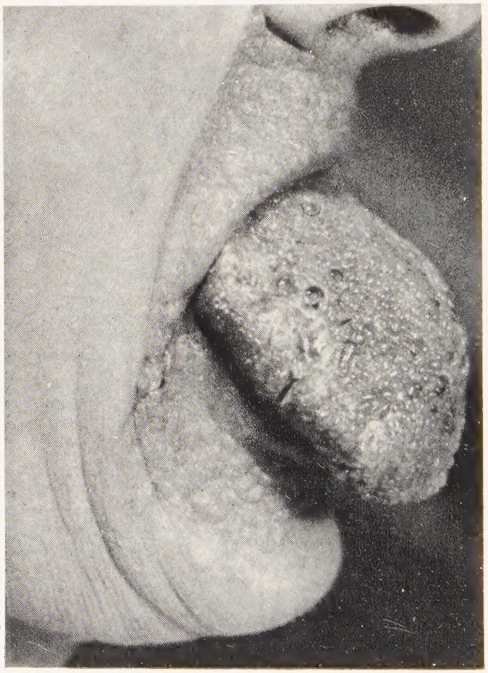

Fig. 1.

on account of breathlessness and pain in the chest. There had been severe attacks of vomiting, and diarrhoea alternating with constipation. Another distressing symptom was severe pain in the right shoulder radiating down the arm to the fingers. This pain was not related to exertion, and often woke her at night.

Clinical findings.—The patient is a thin, anxious woman. Weight 9 stone (57·3 kg.).

The tongue is enlarged (Fig. 1), and its movements are restricted so that speech is indistinct and swallowing difficult. Its surface is studded with papules which obscure the normal papillae ; these papules are brownish and glistening, some of them being haemorrhagic. The tongue is rubbery on palpation and its muscle bulk is increased about three-fold.

The lips are infiltrated and fissured, and the skin from the lower lip to the chin, and from the upper lip to the nose, is covered with almost confluent waxy papules and nodules, which are smooth and translucent like vesicles ; they are pinkish yellow to brown, with some haemorrhages among them (Fig. 2). Similar papules

are present at the vestibule of the nose and at the inner canthi of the eyelids and the external ear passages are almost occluded by nodules.

The skin of the axillae, of the umbilical region and round the anus and vulva shows similar thickenings with papules and nodules. On the palms and palmar aspects of the fingers there is diffuse thickening with deep miliary papules. The subcutaneous tissue over the body is wasted and there is some irregular nodulation in its substance.

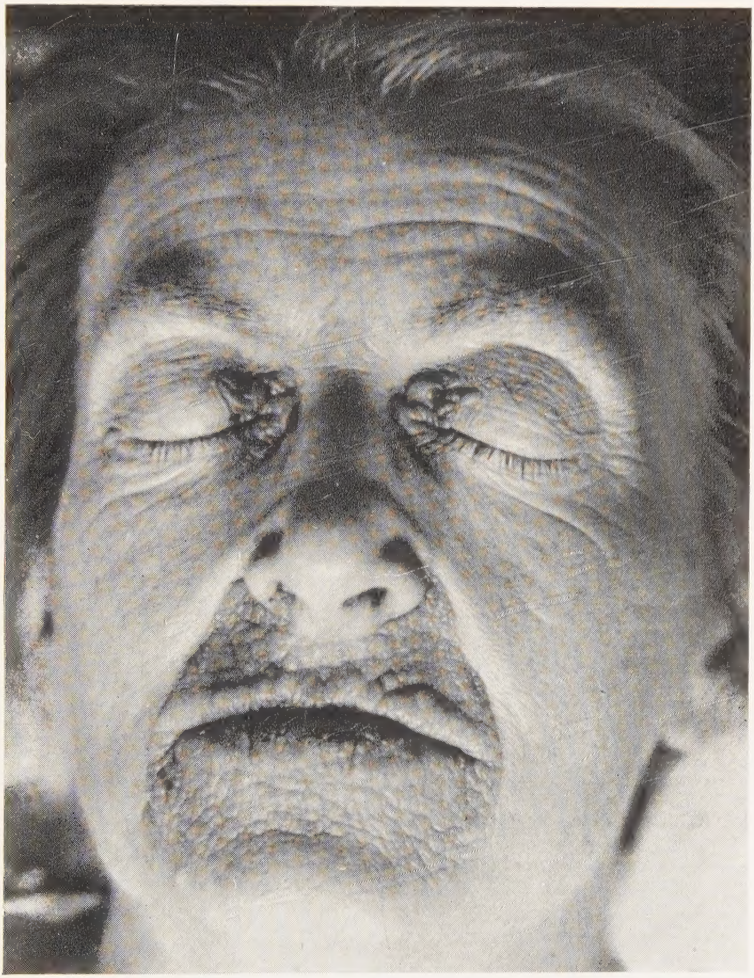

Fig. 2.

There is breathlessness on exertion, with slight congestion of neck veins, oedema of ankles and râles at the lung bases, indicating early cardiac failure. The pulse is regular and the blood pressure is 120/75. The fundi are normal.

The liver edge is just palpable, but other abdominal organs are not felt. The abdomen is distended and tympanitic.

There is muscular weakness throughout the body, with wasting. Movements of the right shoulder are limited by pain. There is ill-defined blunting of skin pain sensation in the right arm and hand ; otherwise the nervous system appears normal.

Investigations.—Biopsy from the skin of the chin (7 June 1950). The epidermis is thinned over hyaline masses that have replaced the papillae (Fig. 3). In some parts of the section this hyaline material extends throughout the dermis, and some of the capillaries are partly occluded by it (Fig. 4). The amyloid material stains faintly

FIG. 3.—Biopsy from skin of chin. Amyloid in papillae stained with Congo red.

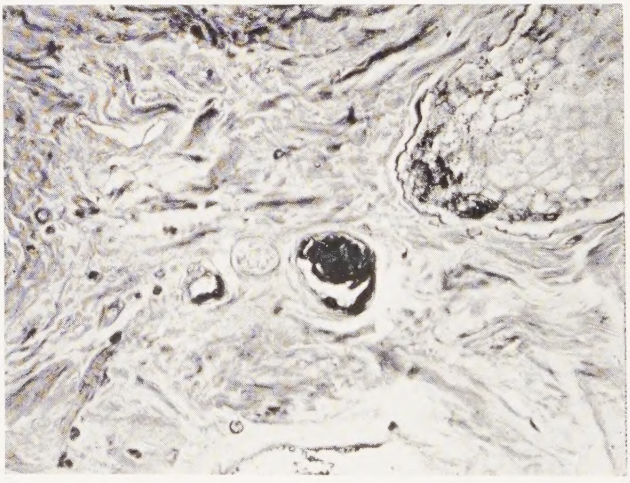

FIG. 4.—Skin biopsy. Small blood vessel in the dermis shows partial occlusion from amyloid in its wall. (Periodic acid-Schiff.)

pink with eosin and metachromatically with methyl violet. With difficulty, selective staining with Congo red was obtained in some sections. The amyloid stains strongly with the periodic acid-Schiff technique.

On 19 June 1950 0·5 ml. of 1% Congo red was injected intracutaneously among the papules in an axilla. After a week the Congo red had diffused through a radius of one inch beyond the site of injection and had selectively stained the tiny amyloid

papules. A biopsy was made from this region on 29 June 1950, and pinkness of the amyloid in the skin could be seen without further staining.

Urine : Repeated examination of urine showed no Bence-Jones protein. There was a trace of albumin, but no sugar. Filter-paper chromatogram of the urine showed no abnormal amino-acids.

A sternal marrow puncture was made on 7 July 1950 :

	%		%
Neutrophils	18·8	Reticulum cells	0·0
Eosinophils	1·2	Proerythroblasts	0·2
Basophils	0·0	Normoblasts (early)	1·6
Lymphocytes	2·0	Normoblasts (intermediate)	4·4
Monocytes	0·4	Normoblasts (late)	5·6
Myelocytes	8·4	Megaloblasts	0·0
Blast cells	0·2	Undetermined cells	0·0
Plasma cells	57·2	Megakaryocytes present in normal numbers.	

Blood counts were normal apart from a progressive secondary anaemia. Platelet count, bleeding time, and clotting time were normal. Blood Wassermann reaction was negative. Blood urea was 30 mg. per 100 ml. Erythrocyte sedimentation rate was 30 mm. in the first hour (Westergren).

Serum proteins : Estimation of serum proteins by the standard laboratory method was normal (albumen 4·3%, globulin 1·5%, A/G ratio 2·9).

Electrophoresis of serum protein (Tiselius) showed excess of beta globulin with mobility nearer to gamma globulin than normal beta, the general appearance of the pattern being reminiscent of myelomatosis.

	%		%
Albumen	45	Beta globulin	33
Alpha globulin	13	Gamma globulin	8

Skiagrams of the skeleton showed no evidence of bone disease.

Skiagram of the chest showed some enlargement of both ventricles, and congestion (or possibly infiltration) of the finer branches of the pulmonary arteries.

Electrocardiographs showed low-voltage deflections in all leads.

Progress.—On account of congestive cardiac failure the patient was confined to bed with restricted movement. There was, at first, some improvement on symptomatic treatment, but in later months breathlessness and dependent oedema progressed.

The pain in the right shoulder troubled her much during the first weeks in hospital, but gradually receded. Attacks of diarrhoea became more frequent, and at times there was abdominal distension and vomiting, suggestive of partial intestinal obstruction.

In view of the finding of plasma-cell myeloma, a course of urethane was given over four weeks, with total dosage of 74 g.

There was no fever throughout the course of this illness. The patient became increasingly exhausted and died in cardiac failure on 20 December 1950, after six months in hospital.

Autopsy.

Heart : The myocardium was thinned in some places and appeared firm and pale. At the apex and in the posterior interventricular septum the myocardium was glassy with amyloid deposits. The endocardium was yellowish-white from deposits beneath it. The valves were healthy throughout and the coronary vessels showed no disease.

Sections of the myocardium showed extensive replacement of muscle by amyloid, and many small blood-vessels had amorphous amyloid material in their walls (Fig. 5).

Alimentary canal: The tongue was covered with amyloid papules below its mucosal surface. The muscle was firm and pale, and sections showed replacement of muscle fibres and obliteration of many blood vessels by amyloid. The oesophagus was thickened. The stomach was enormously distended from partial obstruction at the pylorus through amyloid thickening of the pyloric antrum. The walls of the large intestine were thickened, and the sigmoid colon showed very gross amyloid infiltration.

The liver, spleen and kidneys were macroscopically normal, although sections showed amyloid in the walls of small vessels to a limited extent in all of them.

Lungs: The lungs showed terminal congestive changes and microscopic amyloidosis of small vessel walls. The ductless glands showed no abnormality.

FIG. 5.—Heart muscle. Amyloid degeneration in wall of small blood vessel. (H. & E.)

Bone marrow: The bone marrow was macroscopically normal. Unfortunately, tissues were fixed in formalin and decalcified, so that plasma-cell cytoplasm staining was unsatisfactory. From nuclear appearances it was concluded that there was not more than 10% of plasma cells in the marrow.

DISCUSSION.

This patient had severe, deep pain in the right shoulder and arm of a kind that is rather characteristic of this disease. Navasquez and Treble (1938) described amyloid changes in nerve trunks and in ganglia, and it is possible that our patient had a degenerative neuritis of this kind. Alternatively muscle changes may account for such pains, and in any case there was extensive weakness and wasting and infiltration of skeletal muscles.

The serum proteins were normal by the standard laboratory method, but electrophoresis showed excess of an abnormal beta globulin, such as may be found in myelomatosis.

As is usual in cases of this kind, there was some difficulty in demonstrating metachromasia of the amyloid in skin sections and post-mortem material. Staining with methyl violet produced transient metachromasia and some sections were stained selectively with dilute Congo red, but this was not uniform throughout the tissues. Injection of Congo red into the skin produced vital staining of very small amyloid papules, and this technique may be of some help in diagnosis (Nomland, 1936). The amyloid material was strongly stained with the periodic acid-Schiff technique, which indicates some insoluble polysaccharide component (Hass, 1942). Experimental amyloid in various animal species shows variation in differential solubility, and staining variations are not unexpected (Hass *et al.*, 1943).

There was no radiological evidence of bone disease, but a sternal marrow smear showed 57% plasma cells. This finding is contrasted with the post-mortem observation of no macroscopic changes in the bone marrow, and no microscopic evidence of plasma-cell tumour, plasma cells amounting to not more than 10% of the marrow cells.

We have, then, evidence of plasmocytosis of bone marrow, which was neither progressive nor destructive of bone, and with it there was an abnormal serum beta globulin and deposition of atypical amyloid in mesenchymal tissues. One hesitates to accept this as a myeloma in the sense of a malignant tumour of marrow cells and would suggest a reactive increase in marrow plasma cells, possibly related to some disturbance of the immunity mechanism. Barr (1950) puts forward this view in considering some of the doubtful cases of myelomatosis in his discussion on the function of the plasma cell. It can be accepted that the ribose nucleic acid in the cytoplasm of plasma cells is directly related to cytoplasmic protein synthesis (Caspersson *et al.*, 1941). There is evidence from experimental work in animals (Fagraeus, 1948) of a relationship between the production of antibodies and the number of plasma cells. In rabbits being immunized to horse serum or to typhoid bacilli, reticulum cells increase in the spleen and differentiate towards plasma cells, and the peak of antibody titre follows the appearance of the greatest number of immature plasma cells.

Cases of disordered protein metabolism have been described in relation to known hypersensitivity. Robertson (1950) reports two cases of sensitivity to sulphadiazine in which there were plasmocytosis of marrow and abnormal circulating globulins, and the case described by Baker *et al.* (1949) with amyloidosis and plasma cell increase in lymph nodes may have been related to a sensitivity to milk proteins.

Whether cases such as ours be classified with true myelomatosis or with disorders of immunity, there is increasing evidence of abnormal protein synthesis in bone marrow. Heilmeyer (1950) reviews the "dysproteinoses," and emphasizes the great variety of abnormal globulins that are being encountered with more refined methods of serum protein analysis, particularly in diseases

of marrow cells. In his case of atypical amyloidosis with myelomatosis he describes metachromatic " inclusions " in the marrow plasma cells, and claims that these are in fact amyloid being formed in these cells.

Summary.

A case of primary systematized amyloidosis is described with papular amyloidosis of skin, amyloid macroglossia and extensive gastro-intestinal involvement. Death was from myocardial failure.

There was an increase of plasma cells in the bone marrow, and the significance of this is discussed with reference to disorders of protein synthesis.

I wish to thank Dr. W. N. Goldsmith for permission to publish this case, and for his help in the preparation of this paper. I am indebted to Dr. W. Freudenthal for help with the histological sections.

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HISTOLOGICAL CHANGES IN THE TONOFIBRILS IN VESICULAR AND BULLOUS DISEASES OF THE SKIN.

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INTRODUCTION.

In dermatological histopathology little attention has so far been paid to changes in the epidermal tonofibrils. This lack of interest is due, among other things, to the fact that special staining methods are required, such as Masson's trichrome stain or the saffranin-waterblue-orcein method of Unna. Special optical methods, such as phase-contrast or polarization microscopy can also be used (Fig. 1, B). Our knowledge of normal tonofibrils is still incomplete ; on many points opinions differ.

It is generally assumed that the tonofibrils (*Epithelfasern*, *Protoplasmafasern*, *filaments épidermiques*, *filaments d'union*) are fibrous structures lying in the cytoplasm of the squamous cells and forming protoplasmic cellular bridges from one cell to another, crossing the intercellular lymph-spaces. The connecting bridges (plasmodesmata) each show a small thickening in the centre—Bizzozero-Ranvier's corpuscles. Most authors contend that the tonofibrils pass uninterrupted from one cell to another all the way from the basal cell layer to the stratum corneum ; and they connect the cells of the basal cell layer with the underlying corium. In the cylindrical basal cells they ascend perpendicularly as fine, straight, almost parallel fibres ; in their further course towards the stratum corneum they diverge, approaching the surface of the skin in gradually flattening parabolas. This course clearly depends upon the gradually increasing flattening of the pavement cells towards the surface.

Little is known about the origin of tonofibrils. Favre (1937, 1946, 1950) holds that they are mitochondrial in nature, because they stain like mitochondria by the Regaud-Altmann method, but clearly such evidence is not enough. On the other hand, it seems beyond doubt that mitochondria, which represent the metabolic centres of the cell, must play an essential role in building up tonofibrils. Derksen and Heringa (1937), using Roentgen spectrography, demonstrated that tonofibrils consist of keratin. These findings agree with data obtained with the polarization microscope concerning keratin and tonofibrils. From these facts it is concluded that the tonofibrils make up the keratin masses which arise in the process of cornification. Pathological changes in the tonofibrillar apparatus have been described by Civatte (1943) and by Dupont and Piérard (1949) as occurring

in the course of the process called acantholysis. By this term, chiefly used by French dermatologists, is meant the disappearance of the cell bridges containing the intercellular tonofibrils, with consequent loosening of the squamous cells from their mutual connections.

Material and Methods.

Biopsies from cases of pemphigus vulgaris and a number of other diseases, including dermatitis herpetiformis and experimental bullous dermatoses, were

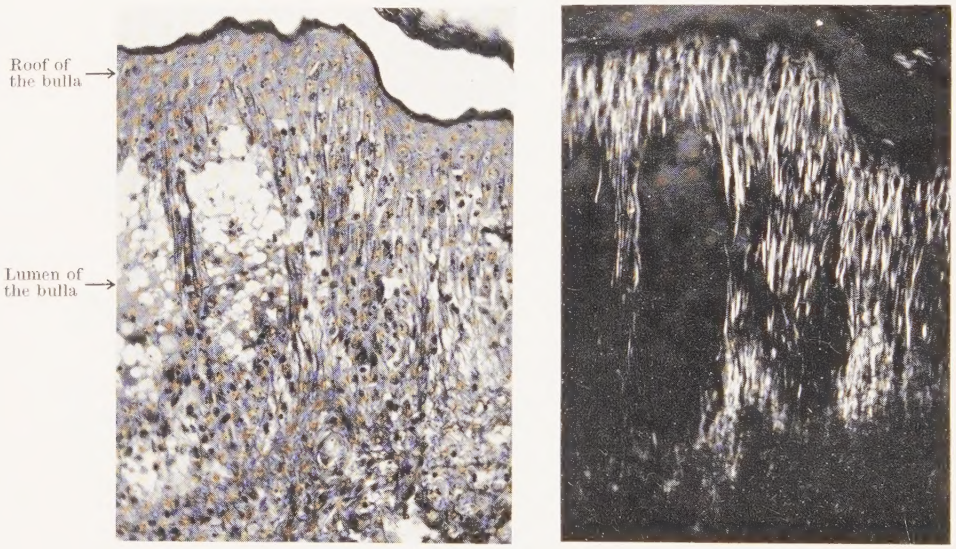

Fig. 1.—A: ordinary bright field. B: between crossed polaroid filters. Pemphigus vulgaris: side-wall of intraepithelial bulla with vertical accentuation of tonofibrils. × 160. (Masson).

fixed in Bouin's solution, embedded in paraffin and stained with Masson's trichrome stain. In addition unstained as well as stained sections were studied with the phase-contrast and polarizing microscope.

Observations.

Normal Skin.

Examination of normal skin did not reveal any deviation from the generally accepted pattern. It was noticed that in occasional cylindrical cells of the basal layer the tonofibrils coalesced to form thicker undulating bundles. These apparently are the spirals described by Herxheimer in 1889. The appearance of these spirals varied considerably.

FIG. 2.—1st phase: intraepithelial oedema in the lower layers with slight accentuation of tonofibrils. × 700. (Masson).

FIG. 3.—2nd phase: clumping of tonofibrils in the side-wall of a bulla. × 700. (Masson).

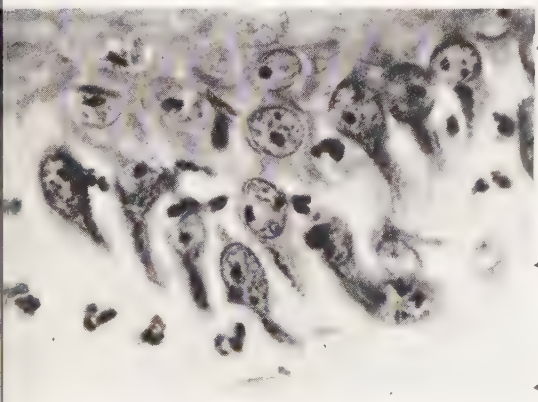

FIG. 4.—3rd phase: spiraling of clumped tonofibrils in Malpighian cells of the roof of a bulla. × 550. (Masson).

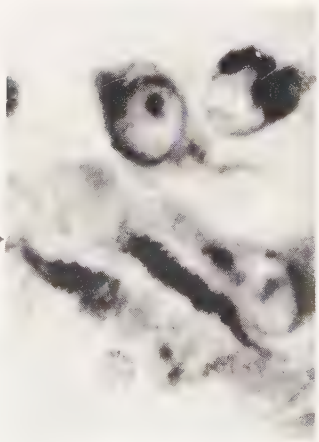

FIG. 5.—3rd and 4th phases: spiraling of tonofibrils in basal layer; tonofibrillary masses in acantholytic cells. × 700. (Masson).

Pemphigus vulgaris.

Of three patients with the clinical diagnosis of pemphigus vulgaris the sections showed intra-epithelial bullae accompanied by the isolation of many epithelial cells in the floor, walls and roof of the bullae (" acantholysis "). The formation of intra-epithelial bullae implies tearing of the cell bridges, and the intercellular tonofibrils of a number of cells were indeed found impaired. It appeared that alterations had also taken place in intracellular* tonofibrils.

A gradation from slight to severe changes in the tonofibrillar system could be traced as follows :

(i) During the stretching of the epidermal cells by intercellular oedema the intracellular parts of the vertical tonofibrils became more clearly visible. We could not decide whether this accentuation was due to hypertrophy or to compression of the fibres in the stretched-out cell (Fig. 2).

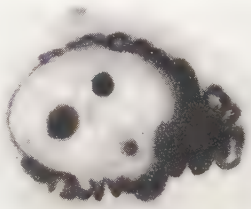

FIG. 6—4th phase : clumped tonofibrillar mass in acantholytic cell.

(ii) As the stretching continued the fibrils coalesced into clumped bundles (Fig. 3).

(iii) When oedema progressed to the formation of bullae, i.e., when tearing took place in the epithelium, retraction of the cells lining the cavity followed and the course of the clumped bundles of tonofibrils became undulating. Thick spirals resulted, staining dark red (Masson), in which separate tonofibrils could no longer be recognized. Individual tonofibrils could still be seen, however, on the side of the cell which was still attached. Here the spiral broke up into separate tonofibrils which passed on to adjacent cells (Fig. 4). In one cell usually only one clumped spiral was found (Fig. 5).

These changes were first seen in the side wall of the bulla. When the bulla extended they were also found in its roof and in its floor.

(iv) At a later stage the thick clumped spiral changed into a circumscribed dark red mass lying next to the nucleus in the cytoplasm (Fig. 6).

(v) Finally the mass fell to pieces.

* Although this name is incorrect, as strictly extracellular parts of the tonofibrils do not exist, the current distinction of intracellular and extracellular tonofibrils will be maintained.

The series of changes described here was absent in those parts of the epidermis where oedema or the formation of bullae did not occur.†

Other Vesicular and Bullous Conditions.

Changes in the tonofibrils identical with those described here in pemphigus vulgaris were, although to a less extent, found also in the intra-epithelial bullae of pustular psoriasis, herpes zoster, and particularly in experimental croton-oil dermatitis. In the last-named, the "acantholytic" cells observed were indistinguishable from those found in pemphigus vulgaris (Civatte, 1949).

In the *subepithelial* bullae of four patients suffering from Duhring's disease we found comparable anomalies of the tonofibrils in the side walls and the roofs of the bullae. As tearing of the bundles of tonofibrils does not occur, the changes were limited to stretching and accentuation.

Discussion.

Dupont and Piérard were the first to describe accurately changes in the tonofibrillar system similar to those we have observed. They contend that these changes are brought about by a primary degeneration of the tonofibrils characteristic of pemphigus vulgaris, leading to the formation of bullae which are invariably intra-epithelial. The histological changes observed by us do not, in our opinion, allow such a conclusion without comment, for we found a similar picture in other conditions characterized by intra-epithelial bullae. Moreover there is an exact correlation between the degree of tonofibrillary change and the amount of mechanical stress exercised on the individual cells. This leads us to suppose that mechanical stresses are responsible for the tonofibrillary changes. The fact that the anomalies are restricted to the walls, roof and floor of the bullae, both in pemphigus vulgaris and in the other conditions with intra-epithelial bullae investigated, supports this view. The same applies to the occurrence of comparable tonofibrillary anomalies in the walls and the roofs of subepithelial bullae in a number of other dermatoses, particularly Duhring's disease.

We have not found any morphological change in the tonofibrillary apparatus which would support the hypothesis that a primary degeneration of tonofibrils is the essential factor in the formation of intra-epithelial bullae in pemphigus vulgaris.

We think it important to point out that the tonofibrillary changes described in this article cannot explain the differences in the extent of epidermal disintegration in the dermatoses examined and the differences between one case and another.

† In pemphigus vulgaris changes of the nuclei and the cytoplasm ran parallel with the tonofibrillar anomalies—the nucleus was swollen and had a coarse chromatin structure; the nucleoli were large; the cytoplasm showed a characteristic light blue colour, except for the dark red tonofibrils (Masson).

Summary.

Tonofibrillary changes observed in the formation of intra-epithelial bullae in cases of pemphigus vulgaris are described. Similar, though less extensive, changes were found in other diseases in which intra-epithelial bullae occurred (among others pustular psoriasis, herpes zoster, and particularly in artificially-induced croton-oil dermatitis).

It is concluded that mechanical influences are chiefly responsible for these changes.

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THE STAINING OF THICK SECTIONS OF SKIN.

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By the middle of the nineteenth century, the basic micro-anatomical structure of the skin had already been elucidated, largely from the study of freehand sections which were necessarily thick. Present-day drawings of such structure are mainly copies of earlier drawings made from these preparations. From the thin sections now in universal use it is difficult to obtain a complete and three-dimensional concept of the layout of hairs, sweat glands, papillae, etc.

The cutting of thick (500μ) sections presents no difficulty, but it can only be done after embedding in celloidin, or better in low viscosity nitro-cellulose (Chesterman and Leach, 1949). A sledge or sliding microtome is necessary. The staining of such sections is not easy because most dyes do not penetrate sufficiently fast, stain evenly enough, or give a sufficiently precise or transparent coloration to the tissues. Of several dyes that were investigated, anthracene blue was the only one that was satisfactory. This method of staining has been published elsewhere (Leach, 1951), but is given here with modifications which make it more suitable for sections of skin.

Examination of the sections should be made with the aid of a Greenough (stereoscopic) binocular dissecting microscope having a matt glass stage. Such instruments cost about £60. Suitable magnifications are × 10 to × 50.

Method.

Embedding.

(1) Fix the skin in formol saline for 24 hours. If it is large, pin it out on a cork plate to keep it flat.

(2) Dehydrate thoroughly in ascending grades of alcohol. This will require 2–4 days.

(3) Treat with equal parts of absolute alcohol and ether for 12–24 hours.

(4) Soak for 2–5 days in 5% nitrocellulose solution made by diluting 1 part of stock nitrocellulose solution with three parts of a mixture of absolute alcohol and ether.

Stock solution of nitrocellulose :

Low viscosity nitrocellulose (E. Gurr) .	140 g.
Absolute alcohol	210 c.c.
Anaesthetic ether	250 c.c.
Celloidin (G. T. Gurr) . . .	4 g.

Dissolve the celloidin first.

(5) Soak for 2–5 days in 10% nitrocellulose solution.

(6) Soak for 2–5 days in stock nitrocellulose solution.

(7) Embed in a paper box containing stock nitrocellulose solution.

Place in an empty desiccator and harden off slowly (about 4 days) until there is only a slight "give" to the block (for more precise details of this stage see Chesterman and Leach, 1949).

(8) Harden the block in 75% alcohol for 2 days.

(9) Trim, and mount on a completely dry wooden block with the aid of some stock nitrocellulose solution. Keep the block, but not the wood, moistened with alcohol for 15 minutes. Then harden and store the whole in 75% alcohol until required for cutting.

Cutting and Staining.

(1) The sections must be cut on a sledge or sliding microtome. They can be cut dry. They can be held with fingers or forceps whilst being numbered with indian ink. The sections should be collected and stored in 70% alcohol.

(2) Transfer to distilled water, one change—$\frac{1}{2}$ hour.

(3) Treat with 5% aluminium sulphate—$\frac{1}{4}$ hour.

(4) Stain for 2–4 days in dilute anthracene blue. (Stock anthracene blue solution, 1 part; aluminium sulphate, 5% solution, 20 to 50 parts. Filter after dilution.)

Stock anthracene blue solution:

Anthracene blue (C.I. 1062. G. T. Gurr)	0·5 g.
Aluminium sulphate, 5% solution .	100 c.c.

Boil for 20 minutes. Allow to cool. Filter next day.

(5) Rinse in 5% aluminium sulphate—1 minute.

(6) Rinse in 2 changes of distilled water—1 hour.

(7) Treat with tap-water—2 to 12 hours.

(8) 70% alcohol—5 minutes.

(9) 90% alcohol—$\frac{1}{2}$ hour.

(10) 96% alcohol—$\frac{1}{2}$ hour.

(11) Absolute alcohol (one change)—$\frac{1}{2}$ hour.

(12) Absolute alcohol and ether (equal parts) (2 changes)—$\frac{1}{4}$ hour.

(13) Xylol (two changes)—$\frac{1}{2}$ hour.

(14) Mount in neutral mounting medium (Flatters and Garnet).

If it is necessary to hold separate pieces together or to mount numbered serial sections, the removal of the nitrocellulose in stages (9) and (10) must be avoided by substituting absolute isopropyl alcohol for these two stages.

Results.

This method gives a precise but transparent nuclear stain and some cytoplasmic staining. If sufficiently dilute anthracene blue is used there is little general staining.

In sections made in the ordinary vertical plane it is possible to confirm and get an excellent impression of the usual description of the micro-anatomical structure of skin. Thus complete sweat glands together with their ducts can be seen in a single section (Fig. 1) ; hair follicles with their associated sebaceous glands and arrector pili muscles can be seen in their entirety. Presumably micro-anatomical abnormality of such structures would be more readily

Fig. 1.—Skin of human leg ; × 30. Stained with Anthracene blue. 500 μ section. To show sweat gland and duct.

detectable than in corresponding thin serial sections. In several pieces of skin that I have examined, one or two small vesicular structures (100μ diameter) can be seen in some sections. If these pieces of skin had been sectioned at 10μ, very few sections would have shown these structures and they would probably have been missed. It was also apparent in one section that the vesicle was the termination of a sweat gland. It would have been impossible to make this observation in thin sections without resorting to the laborious method of wax model reconstruction of several sections.

Some of the most interesting preparations made have been sections cut in a plane parallel to the surface (horizontal sections). They are much more informative than thin sections in the same plane, but it must not be thought that it is easy to get the maximum information from such thick sections.

Observation is tedious, and involves using the eye to the limit of its resolving power. Use of higher magnifications diminishes the optical depth of focus and introduces greater optical blurring of the image. Having observed the pattern it is then necessary to mentally reconstruct the third dimension, and in this one is aided by the inevitable slight obliquity of the section. It may also be necessary to have a section made in the usual vertical plane. Use of plasticine to make crude models is most helpful.

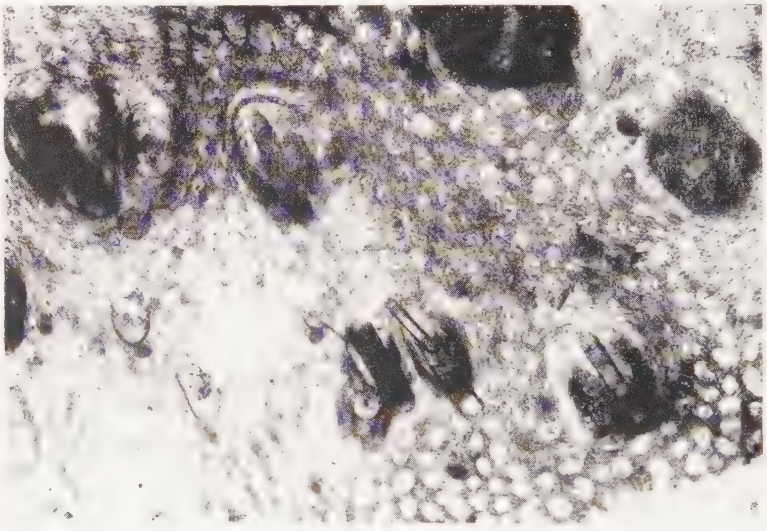

FIG. 2.—Skin of human scalp; × 30. Stained with Anthracene blue. 500 μ horizontal section. To show "collars" round openings of hair follicles and also rete Malpighii seen from above.

I have not studied a large range of normal pieces of skin and have examined few abnormal ones. So the following observations are neither complete nor final:

(1) In the scalp, hairs may emerge separately or up to four may come through the same opening. There is a thickening of the epithelium around the opening (Fig. 2). According to Ramalingaswami (1951) the region of this "collar" is subject to change during avitaminoses.

(2) Frequently two or more separate sebaceous glands open into one hair follicle. In thick horizontal sections of the scalp these may be seen to nearly encircle the hair follicle.

(3) No evidence was found for the concept of rete "pegs." It seems that cone-shaped dermal papillae indent the inner surface of the epithelium. The papillae are so closely set that only thin *partitions* of epithelium separate the papillae (Figs. 3 and 4). It is as though the dermal papillae were surrounded

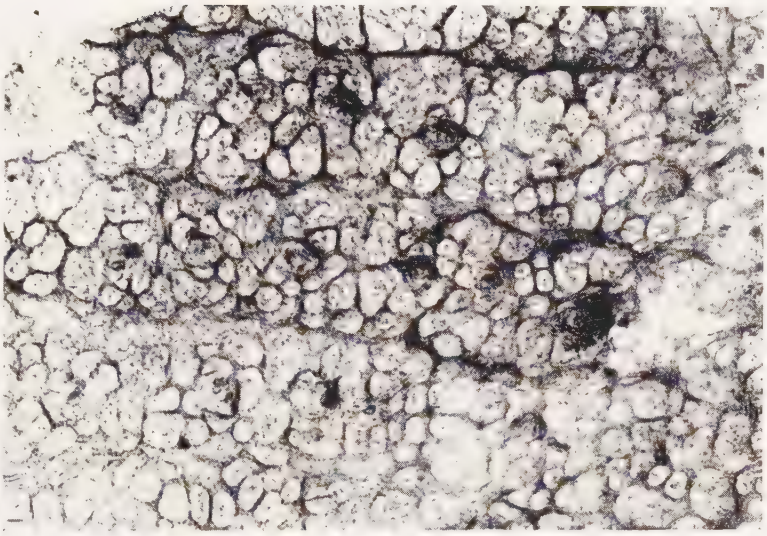

FIG. 3.—Skin of human leg; × 30. Stained with Anthracene blue. 500 μ horizontal section. To show rete Malpighii seen from below.

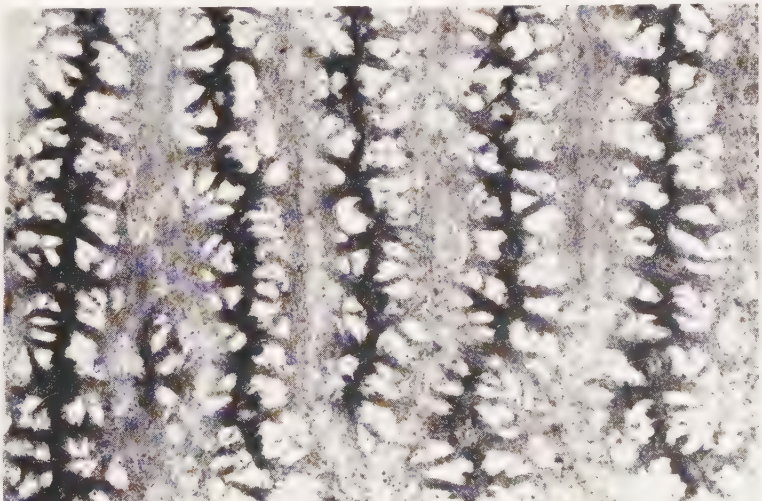

FIG. 4.—Skin of sole of human foot: × 30. Stained with Anthracene blue. 500 μ horizontal section. To show rete Malpighii seen from below.

by flexible plastic cups set upside down and squeezed together until their sides touched. In thin vertical sections the walls of these cups will be sectioned to give the appearance of " pegs " although in reality they are partitions.

This appearance conforms to the description given originally by Malpighi. The network of partitions is the rete Malpighii : so the term rete " peg " is self-contradictory. By the end of the nineteenth century the fallacy of the rete " peg " had already appeared (Klein and Noble Smith, 1880), owing

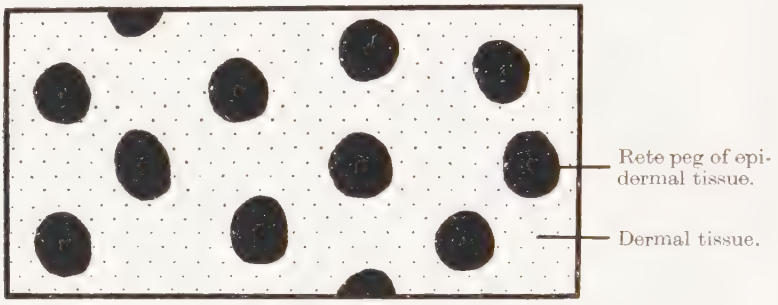

Fig. 5.—Appearance that would be given if hypothetical rete " pegs " were sectioned in a horizontal plane.

Fig. 6.—Appearance that is in fact seen in horizontal sections through the dermal papillae.

presumably to the increasing thinness of the sections then being cut. But Schafer (1898) still gave an accurate, detailed and vivid account ; Stohr (1898) gave an excellent drawing of the rete Malpighii. In some of the French and German textbooks of histology the true description persists (Bouin, 1932 ; Branca, 1921 ; Patzelt, 1946 ; Stohr, 1951). Cowdry (1950) also describes the true structure.

Summary.

(1) A method is described for cutting and staining thick (500μ) sections of skin.

(2) Some observations are made of the type of micro-anatomical structure of skin that can be seen by this method.

(3) It has been confirmed that the lower surface of the epidermis forms a network (rete) of partitions which separate the dermal papillae from one another. No evidence was found for the presence of rete " pegs."

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THE MAKING AND FITTING OF PLASTIC NOSES.

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From the Dermatological Clinic and Policlinic of the State University, Leyden, Holland.

SINCE previous descriptions (Simons, 1937 ; Siemens, 1938) of the making and fitting of plastic noses our technique has considerably improved. In view of the keen interest shown on many sides in the subject, we believe an account of the present state of progress in this respect will be both useful and interesting.

Secrecy in regard to therapeutic methods or medical technique has been maintained, especially in respect of plastic nasal surgery, for a fairly long time. A certain surgeon is supposed to have performed his cosmetic facial operations in mysterious isolation, while another let out just enough about his prothesis to avoid losing any colleagues, and just not enough to recruit competitors. This was the experience of Jacobson (1928), who found himself compelled to build up his own technique from insufficient and vague communications.

For the past twenty years artificial noses have been made at our Leyden clinic, according to a gradually and increasingly improved combination of methods, gathered both from the literature and from our own experiments. These noses fully satisfy the demands made of a sound and cosmetically good prosthesis.

The majority of people requiring an artificial nose are lupus patients ; but there are also cases of congenital lues and trauma that may be eligible. It need hardly be emphasized that the morbid process which has mutilated the nose must first be completely cured before a plastic nose is fitted.

TECHNIQUE.

The patient lies on an operating table or stretcher. A small cardboard "wall" five or six centimetres high is placed on the patient's face, over the upper lip, and enclosing the cheeks and the eyes, so as to allow a clear view of the face. The part of the cardboard which rests on the upper lip is cut so as to fit exactly. The eyes are covered with pieces of gauze which have been soaked in oil of sesamum, and the nostrils plugged with cotton-wool. Should there still be any space between the skin and the cardboard "wall," it should be carefully filled up on the inside with a strip of wet cotton wool, and fixed on the outside with adhesive plaster.

Into this "mould" the negative of the face is then cast, with Dr. Poller's "Negocoll."* This Negocoll, to which a little water has first been added, is boiled up until

* Obtainable from Dr. Poller's Negocoll, Apotela Manufacturers, Zurich, Switzerland.

it becomes a thick, smooth liquid mass ; this takes about half an hour's continuous stirring, after which there should not be the smallest lump left. The Negocoll is now rapidly cooled down to 40° C., and carefully poured into the cardboard "wall" and on to the patient's face. Care should be taken to avoid the Negocoll getting underneath the "wall" and into the patient's mouth, since he can breathe only through the mouth during this process. (We give the patient a short -not too narrow- tube to breathe through.) Pouring should not be done too slowly, otherwise the Negocoll will cool too much, and spoil the result.

The patient remains in this position, with the plaster on the face, for half an hour. The Negocoll has now cooled down and the negative is readily removed from the face. It does not adhere to the eyebrows or eyelashes.

The plaster-of-paris positive is now at once poured into the Negocoll negative. After this the Negocoll can be put through a mincing-machine, kept in an hermetically sealed bottle, and used again.

The plaster-of-paris positive is now painted with a shellac solution, and left to dry for a day or two. It is then possible to model the missing (part of the) nose in ordinary modelling clay. To get the right shape to suit the patient's face, one may refer to one of the patient's previous photographs, or to a picture of the nose of a relative to get the family nose. In the case of an ear prosthesis one makes the symmetrical equivalent of the other ear.

For a clear, comprehensive view of the patient's face it is important to make as large a Negocoll negative as possible. Another point of great importance in modelling the new nose is to smear the clay a little beyond the nose where it passes into the cheek, so as to obtain an invisible transition. Nostrils are also made in the model. When the model is quite finished, the whole of it is painted with shellac, and again left to dry for one or two days, after which enough plaster-of-paris is filed away to leave the model nose with ample edges ($1\frac{1}{2}$–2 cm.). This plaster positive, including the modelled nose, is again painted with shellac and left to dry. It is then smeared with oil of sesamum and a plaster-of-paris negative made.

The modelled (clay) part is now removed from the positive, after which the plaster positive and negative are both painted with shellac.

Together, this positive and this negative form the mould. A trial nose is now cast in this mould and fitted on the patient's face. If it fits well, and closely connects up with the existing defect, then the plaster mould is copied in brass (and provided with feet) by a brass-founder.* Such a brass mould is unbreakable and cannot lose its shape. Before the mould is nickel-plated, another trial nose is cast in it, to make sure that the proper shape has not suffered in any way.

The prosthesis is now cast in the nickel-plated mould in the following way :

A small dish is placed in a slightly larger one, so as the make a water bath, and the following ingredients are heated over a tiny flame : 20–30 c.c. glycerine and 2–3 teaspoonfuls of powdered gelatine. This mixture is boiled up, being continuously stirred, into a syrupy mass. To this paste we add half a teaspoonful of precipitate of calcium carbonate, which makes it dull and opaque. We now add as a preservative as much quinine sulphate as will cover a sixpence, and a little cosmetic face-powder or rouge to get the desired colour that will match the patient's complexion. Both halves of the mould have previously been well painted with oil of sesamum. The gelatine mixture is now poured into the mould, which should be firmly pressed together to get the edges as thin as possible and so make the transition from nose to cheek practically invisible. After five minutes the nose may be carefully "peeled" out of the mould. The edges are trimmed with scissors, and the nostrils pierced with a hot knitting needle. "Pores" may be imitated by tiny pinpricks ; for patients with freckles a few of these may also be put on the artificial nose.

* This costs about 35 Dutch florins (£3 10*s*).

FIG. 1.

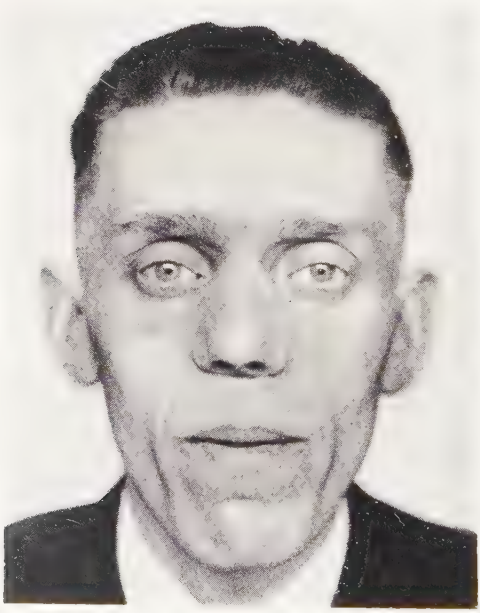

FIG. 2.

The nose produced in this way can be stuck on the patient's face with the aid of a mastic solution, after which the edges may be finished off with a little powder and, if necessary, "ironed out" very lightly with a warm metal spatula.

In most cases such a nose will look perfectly natural (Figs. 1 and 2). (It has even occurred that medical students doing practical work put a speculum in an artificial nose without noticing the difference!) The plastic nose is firmly attached and even able to stand a little pushing about. Its elasticity saves it from undue deformation, while at the same time enabling it to join in the patient's facial movements. Within reason it can stand a fair amount of wind, rain and heat. A walk along the sea-front in summer will do no harm, and we remember a case where the prosthesis, even in the tropics, did not leave its owner in the lurch. The only drawback in a hot climate is that a fresh nose has to be cast every day. Normally one may, of course, cast the noses for a whole week in advance.

Armed with a good prosthesis, the patient need not have the slightest compunction in appearing in public; if there is any hesitation, he should be encouraged not to allow his "rebirth" to make him afraid to face the world again.

If the patient, on account of his occupation, has not the time - or the desire - to make a new nose regularly, he will have to choose between a plastic operation, with less aesthetic but more efficient result, and the cosmetically more successful plastic nose. The former means a series of operations lasting some months; the latter a regularly recurring loss of time of, say, fifteen minutes for each nose. Experience has shown that this question must be studied and solved strictly individually.

Summary.

The technique of making noses is described.

The credit for the practical work is due to this Clinic's analyst, Miss K. Postema, who has attained great skill in it.

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AN UNUSUALLY LARGE DERMOID CYST OF THE SCALP.

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Neurosurgical Unit, Swansea.

It is well known that dermoid cysts frequently arise in the scalp, but it must be uncommon for one to attain the dimensions of the one here described. Such dermoids originate by inclusion of a portion of ectoderm during the process of closure of embryonal fissures. A simple dermoid cyst is a single cyst lined by epidermis, and the cyst wall contains hair follicles, sebaceous glands and sweat glands. Its contents therefore are sebaceous material and a variable quantity of hair. The growth of a dermoid cyst depends upon the secretion from the dermal glands in its wall.

Case History.

On 28 April 1949 the patient, a man aged 35 years, attended the Neurosurgical Out-patient Clinic complaining of a large swelling on his head. At his birth the parents had noticed a small lump on his head in the midline in the region of the coronal suture. This had gradually enlarged with the passage of time until it had reached the present state (Fig. 1). The man was an omnibus driver, and the swelling had become so large and pendulous that it was seriously interfering with his fields of vision.

Apart from the swelling there were no abnormal clinical findings. It was tense, fluctuant and non-pulsatile ; it was not translucent. The scalp posteriorly and laterally was freely mobile over the swelling, but anteriorly the scalp was extremely thin, attenuated and adherent to it.

Radiographs of the skull showed no abnormality apart from what appeared to be a small circular bone defect 1 cm. in diameter at the juncture of the coronal and sagittal sutures. The diagnoses considered were :

(i) Meningocele.
(ii) Encephalocele.
(iii) Large sebaceous cyst.
(iv) Dermoid cyst.

In view of the radiological evidence of a bony deficiency at the site of attachment of the tumour, it was considered desirable to ascertain whether any communication existed between the tumour and the intracranial contents. Air studies of the ventricular system showed ventricles of average size with no shift. There was no evidence of communication between the tumour and the cerebrospinal fluid pathways. The cerebrospinal fluid was normal.

This investigation ruled out as far as possible the possibilities of meningocele and encephalocele, and it seemed that the most likely diagnosis was that of a large dermoid cyst.

Aspiration of the swelling produced thick, yellowish fluid, and on culture this proved to be sterile.

Operation.—On 5 May 1949, through a coronal scalp incision, the swelling was dissected away from the scalp. It was a thick-walled cyst and separated easily except at the anterior pendulous part, where the scalp overlying it was very adherent. At the junction of the sagittal and coronal sutures the cyst was seen to be arising from what appeared to be the circular bone defect noticed in the radiographs. In fact this was a dimple in the skull, the floor of

FIG. 1.

which was a mere flake of bone. The cyst therefore was arising from the plane between the scalp and pericranium.

After all redundant scalp had been cut away the wound was closed with interrupted silk sutures.

The pathological report confirmed that this was a true dermoid cyst, its walls consisting of epidermis in which could be seen sebaceous glands, sweat glands, and hair follicles. The contents of the cyst were sebaceous material and a large quantity of hair.

I treated this patient when I was Deputy Regional Neurosurgeon in Newcastle-upon-Tyne. I would like to thank the Regional Neurosurgeon, Mr. G. F. Rowbotham, for permission to publish the case.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. G. B. Dowling.

15 November 1951.

Sclerosing Lipogranuloma.—Dr. S. T. Anning.

Male, aged 64 (referred by Mr. P. J. Moir), had for several years suffered from tightness of the prepuce with a little difficulty in micturition. January 1951 in the shaft of the penis appeared a painless lump, which slowly increased in size. No history of injury, or of injection, or of taking drugs. In May 1951 the prepuce was slit and a biopsy done.

Past history.—None of note.

Family history.—None of skin disease, diabetes or tuberculosis.

On examination.—A thick plaque is present in the dorsum of the penis about 12 × 6 cm. in size attached to the skin and covered by normal epidermis. It is firm with a well-defined margin and is not tender on palpation. In the scrotum, just before the base of the penis on either side, are two indurated swellings each about 1 cm. across. Around the urethral meatus, which is narrowed and eccentric, the changes resemble balanitis xerotica obliterans. The skin elsewhere is normal. Testes normal. Slight enlargement of inguinal glands. Blood pressure 180/100. General examination (including rectum) otherwise normal.

Investigations.—W.R. negative. Blood picture normal. E.S.R. 24 mm./1 hr. (Westergren).

Skiagrams of lungs and hand bones showed nothing of note. Intravenous pyelography showed nothing abnormal.

Histological examination.—A granulomatous reaction. The superficial corium is densely infiltrated by cells, follicularly arranged, with abundant, often vacuolated cytoplasm and oval vesicular nuclei. Similar discrete follicles patchily infiltrated by lymphocytes and plasma cells lie in the deeper corium and subcutis. Altered fatty tissue shows a widespread necrosis and oedema. The collagen shows hyaline changes.

Comment.—The condition appears similar to that described by H. F. Smetana, and W. Bernhard, (1940, *Arch. Path.*, **50**, 296), as sclerosing lipogranuloma.

Progress.—During the last five months the swelling has not altered. He has occasional difficulty in micturition with the tight urethral meatus, but does not wish for treatment.

Dr. F. F. Hellier: We have recently seen two similar cases. One was a man with the deep type of scleroderma with extensive plaques on the legs and thighs which had been present for many years without altering materially. On re-examining his histological sections we found a picture exactly like the present case: large vacuolated spaces through the dermis, reaching up to the epidermis, with the same curious hyaline changes in the collagen. The other case, recently shown at a clinical meeting by Dr. A. J. E. Barlow of Huddersfield, also showed deep scleroderma-tous plaques and similar histological appearances. I feel these cases must be distinguished from ordinary scleroderma. It is possible that cases may have been overlooked because no biopsy has been taken. The chronicity of the lesion is easily explained by the enormous globules of fat, as it is difficult to see how these could be absorbed. The only possible treatment would be complete excision.

Dr. H. Haber: The condition under discussion involves the midcutis and subcutis. It is interestingthat although the subcutis of the penis never contains fat cells, yet a lipogranuloma

has developed. There is a resemblance to paraffinoma in a "Swiss cheese appearance," but on closer inspection one can see the oil drops surrounded by an ectoplasm with an eccentrically situated flat nucleus. Some drops, however, are surrounded by histiocytes. I have seen a similar picture in scleroderma where there was a marked increase of connective tissue engulfing isolated islands of fat cells from the subcutis.

Dr. Brian Russell: In 1949 I showed a patient with paraffinomata (*Proc., roy. Soc. Med.* **43**, 394), and the somewhat morphoea-like picture resembled that of this patient's lesion making allowance for the differences due to situation.

The President: Has any suggestion about the pathogenesis of these cases been made? I would be interested to know how fat has appeared in a site where normally there is none.

Dr. Anning: Apart from the history of trauma in 3 of the 14 patients reported by Smetana and Bernhard, there seems to be no cause known for the condition. I have gone into the question of injury and the possibility of injection, and I feel that with this particular patient it would be most unlikely that he had either injected himself or been injected by somebody else. It seems to me that short of further biopsy and staining of fat we cannot clear up that point.

Recurrent Phagedaenic Ulcers.—Dr. I. B. Sneddon.

W. B—, aged 52, was admitted to the surgical wards in August 1948 with acute abdominal pain and a history of recurrent dyspepsia for thirty years. Two weeks before admission he had developed acute abdominal pain and pyrexia. A tentative diagnosis of basal penumonia was made but a chest radiograph showed no evidence of this.

Family history.—Nothing relevant.

Previous history.—Duodenal ulcer proved by skiagram twenty-five years ago.

Three weeks after admission several tender indurated nodules appeared on the shins, thighs and left arm. The overlying skin became purple and later ulcerated, leaving ragged necrotic centres. The ulcers continued to extend for many months despite numerous local applications and parenteral penicillin and streptomycin. In February 1950 the ulcers had healed, leaving papery scars. In July 1950 fresh necrotic areas appeared on the legs and in the scars on the thighs. Treatment with diathermy in September 1950 had no beneficial effect.

In December 1950 Chloromycetin 250 mg. three-hourly was given. Within a few days the ulcers began to heal and six weeks later they had almost healed. The Chloromycetin was stopped and the ulcers again began to extend. In February 1951 Chloromycetin was re-started with immediate improvement in the ulcers, which were completely healed a month later.

He remained well until October 1951 when two ulcers appeared on the shins. These are responding to Chloromycetin.

On examination.—There are extensive irregular scars on the left arm, the front of both thighs and the shins. A ragged and granulomatous ulcer is present on each shin. The margins of the ulcers are raised and necrotic. General physical examination has revealed no abnormality.

Investigations.—Histology: Sections from the edge of the ulcers on two occasions have shown only necrosis and infiltration with polymorphonuclear leucocytes. No evidence of polyarteritis nodosa.

Bacteriology: Cultures from the original unbroken nodules and intact pustules which have appeared since were sterile. A penicillin-sensitive *Staphylococcus aureus* has been obtained on many occasions from the ulcerated areas and recently *B. coli* has also been isolated.

No anaerobic organisms or fungi have been found. Blood Wassermann negative. Mantoux test 1 100 positive. The white cell count has varied between 8000-14,000 with a polymorphonuclear leucocytosis. The red cell count has shown no abnormality.

Skiagram of the legs has shown irregularity of the medullary cavity and localized areas of increased calcification in the tibiae.

Comment. The majority of chronic gangrenous ulcers recorded have been of the type described by Meleney (1933) as progressive bacterial synergistic gangrene and have started from the site of an operation or from a traumatic lesion, such as in the

case shown here by Wallace in 1946, or they have been associated with ulcerative colitis or other debilitating disease. Russell (1950), reviewing the literature on pyoderma in ulcerative colitis, noted that 6 of 32 cases started with erythema nodosum-like lesions. There has been no evidence of ulcerative colitis in this case.

Whittle (1945) showed a case of chronic multiple ulcers of twenty-five years' duration in a man of 60 who appeared to be in good health. Hicks (1950) reported a case under the title " Ulcus Migrans " which occurred in a man of 20, who, however, also had acne indurata.

In the present case the onset with fever and abdominal pain and the numerous sterile cultures from the early lesions suggested that the ulceration might be due to a systemic disease such as polyarteritis nodosa. However, the lesions have remained confined to the skin and there has been no evidence of polyarteritis in any internal organs. In chronic ulceration artefact has always to be considered, but these ulcers have been watched from their earliest days and have failed to improve with occlusive dressings, so that artefact can be excluded. There has been no evidence that the ulcers are tuberculous and of the type reported by van den Meer in 1950. It appears that this type of ulceration is a peculiar individual reaction to a common organism, such as a staphylococcus, rather than an infection with a rare organism

The response to Chloromycetin on three occasions suggests either that it is controlling the infection with staphylococci, which have latterly been present in large numbers, or that it is having some specific effect in promoting healing which is not possessed by the other antibiotics that have been used, even though the organisms were sensitive to them *in vitro*.

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Dr. Brian Russell : In phagedaenic ulceration with ulcerative colitis the ulcers only develop when the patient is *in extremis* after a severe bout of diarrhoea or after a massive intestinal haemorrhage. The ulcers heal when the diarrhoea subsides or when the blood loss is made good, unless other factors such as hypostasis or thrombosis are present. At the worst phase there is no leucocytosis, often a frank leucopenia, suggesting that a bone-marrow failure secondary to the blood, salt and fluid loss is responsible for the lack of inflammatory reaction in the ulcers.

Dr. D. I. Williams : A case of mine similar to this followed the same course. The ulcers looked very much like these ; they healed, broke down and healed again over a period of three years. She was admitted to hospital for the last time because an enlarged liver was found and after a month she died. She had the largest tuberculomata in the liver I have ever seen. It seems that this is probably some ordinary organism flourishing in a patient unable to combat it.

Dr. C. H. Whittle : I think the ulcers in my case were not much like the present ones. They were localized to the upper part of the body, the arms and the chest. The patient was much older -he was 60 when he presented himself—and he had had these ulcers for twenty-five years. He had not been near a doctor in that time, so an artefact is extremely unlikely. He failed to respond to most of the antibiotics. The lesions were more like tuberculous ulcers, but biopsy sections did not support this. We were never able to find a satisfactory organism to explain them. We did recover staphylococci and, once, micro-aerophilic streptococci, but they did not seem to be causative. Blastomycosis was mentioned here ; special cultures were made but nothing was found. He was recently given Chloromycetin without the slightest effect. These chronic ulcers give rise to little ill-health and may be unassociated with any systemic changes.

Dr. Oliver Scott : I suggest treatment by the amniotic " graft " technique described by Troensegaard-Hansen (*Lancet*, 1950 (i), 859). By this method leg ulcers of many different causes will heal when they have hitherto obstinately resisted ordinary treatment.

Sarcoidosis.—Dr. I. S. Hodgson-Jones and Dr. C. S. Nicol.

N. M —, male, aged 35, was admitted to an observation ward with euphoria, hallucination and fits in 1938. He was found to have a negative blood Wassermann reaction ; but on the cerebrospinal fluid changes, which were a positive Wassermann

reaction, 155 cells c.mm., and a raised globulin and Lange 2223444321, a diagnosis of dementia paralytica was made and he was treated with malarial therapy.

He was admitted to hospital with epilepsy in 1949, and at that time had nystagmus, exaggerated jerks including jaw-jerk, and bilateral extensor plantaris response. The cerebrospinal fluid changes showed a rise in the protein and cells, and a Lange curve with a mid-zone rise. He was treated with 7 mega units of penicillin and a further 20 mega units were given a year later.

The patient's father had a urethral stricture due to gonorrhoea; however, his Wassermann reaction is negative, as is that of his brother and wife. He has one normal child. At the age of 16 years the patient ran the risk of acquiring venereal infection.

His present condition is that he has had sarcoid lesions on his face, nose and ears for eight months and erythema nodosum on his legs, which is now fading.

His fingers show fusiform swelling. His pupils are irregular and unequal, the reaction to light is sluggish, and on the right retina is an abnormality thought to be congenital.

He has nystagmus and increased deep reflexes, together with some retardation of thought.

Skin biopsy confirmed the diagnosis of sarcoidosis. The Mantoux was positive 1 1000. Skiagrams showed osteitis tuberculosa multiplex cystoides (Jüngling) of the hands, and increased markings in the bases of the lungs consistent with sarcoidosis.

The most recent cerebrospinal fluid examination still shows raised cells and protein levels.

Comments. The diagnosis of sarcoidosis is established by the histology, and further strengthened by the findings in the bones and chest.

The association with erythema nodosum has been frequently described.

The syphilis might be considered as a fortuitous association, or perhaps —by some— as aetiologically significant, or even as non-existent in this case.

The evidence that the patient may have had syphilis rests on the following points: He has had a disease which has diffusely attacked the central nervous system in a way very much resembling the classical picture of G.P.I.: hallucination, euphoria, depression and fits, together with upper motor neurone lesions, and on two occasions the Wassermann reaction in the cerebrospinal fluid has been positive, although the blood Wassermann reaction has never been so, and the cerebrospinal fluid changes, the cells, raised protein and Lange would do well for syphilis.

Against this, however, is that antisyphilitic treatment has failed to change the cerebrospinal fluid abnormality, which I understand is a great rarity.

The serological studies of the patient's relatives in no way support the diagnosis of congenital syphilis.

Sarcoidosis is a condition now well recognized as attacking the central nervous system (Colover, 1948), and in cases previously described the range of abnormalities produced is very wide: meningoencephalitis, myelitis, arachnoiditis, cranial nerve palsies, and peripheral neuritis as well as personality changes.

The cerebrospinal fluid findings may be a pleocytosis, raised pressure and protein, positive Nonne and Pandy tests, and with mid-zone rises in the Lange: but never has there been recorded a positive Wassermann reaction in the fluid as far as I know.

Perhaps not too much importance should be attached to cerebrospinal fluid Wassermann reaction as being specific to syphilis in such a case. non-syphilitic conditions have, on rare occasions, been recorded as giving positive results: for example, in the cerebrospinal fluid of a case of tuberculous meningitis after treatment with streptomycin (Janbon *et al.*, 1951).

REFERENCES.

COLOVER, J. (1948) *Brain*, **71**, 451.

JANBON, M., MOUSTARDIER, G., BERTRAND, L., and SALVAING, J. (1951) *Sem. Hôp., Paris*, **27** (VI), 381.

Dr. C. S. Nicol : When I first saw this patient he had no skin lesions of sarcoidosis but it seemed to me that the response to treatment was not typical of general paresis. I now feel that the patient never had neurosyphilis, the diagnosis of which depended on the results of the spinal fluid Wassermann tests, which were originally reported as " weak positive."

Cell and protein changes in the spinal fluid accompanied by mental symptoms have been reported in sarcoidosis, and it is possible that our patient never had neurosyphilis. It is important to realize that sarcoidosis with involvement of the nervous system can simulate neurosyphilis.

Reference.

Dattner, B. (1949) " Penicillin Failures in Neurosyphilis " *in* Symposium on current progress in the study of venereal disease, p. 93. Div. of Vener. Dis., U.S. Publ. Hlth. Serv., Washington, D.C.

Dr. J. Sommerville : I would suggest that a Kveim antigen test would be of some significance in this case.

Dr. D. S. Wilkinson : If the man has had sarcoidosis since 1938 it is curious that the erythema nodosum lesions should appear only this year. When they do appear with sarcoidosis they are, in the vast majority of cases, at an early stage. It is interesting that they only appeared this year together with the other skin lesions.

Dr. Peter Borrie : I recently saw a case of erythema nodosum with bilateral hilar enlargement, in which liver biopsy showed extensive sarcoid deposits. This widespread hepatic involvement suggested to me that the sarcoidosis was not of recent origin, in spite of the occurrence of erythema nodosum.

Dr. C. S. Nicol : I have seen two patients with undoubted syphilis develop sarcoidosis after full antisyphilitic treatment.

Urticaria Pigmentosa Verrucosa.—Dr. W. N. Goldsmith and Dr. G. C. Wells.

M. A. K—, married woman, born in India (*Eurasian*).

Admitted to Hospital for Tropical Diseases 1 August 1951 under the care of Sir George McRobert, to whom we are indebted for permission to show her.

History. Pigmentation was first noticed in 1945 and has gradually increased since then. The more discrete skin lesions have been appearing over the same time. In the spring of 1951 she developed *diabetes* after an attack of pneumonia. This was followed by *general pruritus*, especially of the vulva. *Since the diabetes has been controlled the pruritus has disappeared.* She has been in hospital on account of old glaucoma, diabetes mellitus and hypertension.

Clinical findings.—Widespread patchy pigmentation over the whole body. The face looks plethoric and the pigmentation here is slaty. In most areas the colour is brownish, and suggestive of melanin. There is no abnormal pigment in the mouth. On the flexor surface of the arms there are conspicuous lentil-sized papules ; they are brownish red and smooth surfaced. Over the abdomen there are pigmented macules which urticate on rubbing, and there are also papules and plaques. The plaques near the navel are almost black and have a rough warty surface.

There is no lymphadenopathy. Liver and spleen could not be felt.

General medical state.—B.P. 270/180. Moderate cardiac enlargement. E.S.R. 12 mm. hr. Typical diabetic blood-sugar curve. Serum cholesterol 280 mg./100 ml. W.R. and Kahn negative. Blood count normal. Old glaucoma. Skiagram of chest shows no lung disease. Afebrile while in hospital. Diabetes controlled on P.Z.I., 10 units daily.

Histopathology. One of the papules on the left upper arm was excised, and a portion of the warty plaque near the navel. In both, the dermis was laden with mast cells, together with some lymphocytes and a few melanophores. Surprisingly, the mast cells were clumped into more of a tumour in the abdominal plaque than in the discrete papule from the arm. The latter showed slight acanthosis and elongation of rete pegs and deep pigmentation of the basal layer. The abdominal plaque showed more acanthosis and also irregular hyperkeratosis with some folding of the surface between warty projections of the epidermis.

Dr. Freudenthal comments :

" Both lesions show typical urticaria pigmentosa, but the verrucous surface is difficult to interpret.

" It might just do for a *verruca senilis*, and, as this has been suggested clinically, I will not exclude it histologically.

" Looking for another interpretation, I thought it might be an epidermal hyperplasia as a reaction to the mast-cell tumour underneath.

" An analogy would be the pseudo-epithelioma over a myoblastoma, the atypical epithelial proliferation, sometimes basalioma-like, over a histiocytoma, and probably also some keratomas over angiomas.

" I have never seen it in urticaria pigmentosa."

R. R. Kierland, and O. C. Stegmaier, (1950) *Arch. Derm. Syph., Chicago*, **62**, 28, describe a large nodular type of urticaria pigmentosa in a baby (almost black elevated plaques). The section showed *hyperkeratosis* over the mast-cell plaque, but the Malpighian layer was thinned and flattened.

Incontinentia Pigmenti (Bloch-Sulzberger). —Dr. C. D. Calnan.

J. P—, female, aged 4.

History.—This child was admitted to hospital in May 1947 at the age of seven weeks. She had an eruption which appeared 2–3 days after birth of grouped vesicles on the right forearm, together with macular and papular lesions on the arms and legs. Over the knuckles and the backs of the fingers of the left hand were hyperkeratotic warty areas. Some of the lesions suggested lichen planus and others a verrucous naevus. Histological section showed hyperkeratosis and acanthosis.

The baby's general condition was unimpaired and no other abnormality was recorded.

She was not seen again until September 1951, when her sister was admitted with the same condition.

Examination. —There is no abnormality except a few flecks of pigmentation on the trunk.

Family history.—See next case.

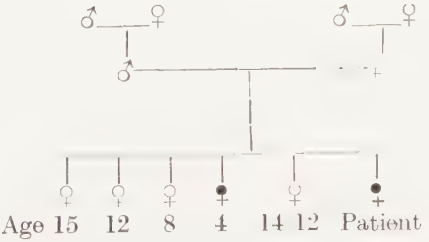
C. P—, female, aged 5 months.

History. When 3 days old an eruption appeared on the legs and arms. No irritation or constitutional disturbance. This eruption was said to be like dermatitis herpetiformis.

She was first seen at hospital when two weeks old with an irregular band of grouped large papulo-vesicles on the arms and legs. The vesicles, 2–5 mm. in diameter, were honey-coloured and apparently full of serum. Some of them were of oval or kidney shape. When four weeks old most of the vesicles had been replaced by violaceous papules of the same irregular distribution; two to three weeks later warty lesions appeared, especially on the dorsum of the thumb and fingers.

Examination.—On the arms and legs there is an eruption of papular and warty lesions of very bizarre pattern, with pigmentation at the sites of previous papules.

Family history:



Dr. Calnan: The first point about these children is that the pigmentation does not parallel the extent or severity of the bullous and verrucose lesions; the elder child had very extensive lesions and yet there is almost no pigmentation present. The next point is that they are females, as is usual. Females preponderate highly in the reported cases. The clinical picture although

diverse and bizarre is none the less characteristic. Recently Dr. Carney of Iowa City reviewed most of the cases in the literature, and pointed out that half of them were reported as having vesiculo-bullous lesions. In some of the older cases it was not mentioned : the younger the child the more frequently were the lesions shown. In Dr. Carney's review half showed the warty lesions. The occurrence of the disease in two members of a family is not very common. Out of 40 cases the familial incidence has only been reported five times, although Dr. Cockayne said in his book that it is an inherited condition.

Dr. H. Haber : The peculiar pattern of the pigmentation is due to pigmentary incontinence of the cells in the basal-cell layer and follows the bullous eruption. The intensity of the incontinence varies and the bullae leave different shades of pigmentation ; some leave no pigmentation. Pigmentary incontinence occurs in many other dermatoses where there is a liquefaction necrosis of the basal-cell layer, such as the poikilodermas of Jacobi and Civatte, lichen planus, lupus erythematosus, erythroderma. Lipomelanic lymphadenopathy is due to loss of pigment into the cutis, from where it is transported into the glands. The verrucous lesions are probably due to the same stimulus that causes the bullous eruption. Incontinentia pigmenti is very often accompanied by other mesodermal and ectodermal defects, and it is reasonable to presume that all the manifestations are due to the same stimulus.

Multiple Naevoid Basal Cell Epitheliomata.—Dr. E. Waddington.

Miss D. S—, aged 52.

History.—In April 1947 the patient came with an ulcer on the right lower eyelid, and another on the left side of the nose. That on the eyelid began a year earlier as a small spot, which gradually increased in size and ulcerated seven months later. She has had a small lump on the nose for over ten years ; recently this has become crusted.

Past history.—No previous illness. No prolonged exposure to sunlight.

Family history.—Nothing relevant.

On examination.—In 1947 the ulcer on the right lower eyelid extended from the inner canthus $\frac{1}{4}$ in. along the margin of the lid. The edge was rolled and semi-translucent. On the left side of the bridge of the nose there was a small pearly telangiectatic nodule with a depressed centre covered with a crust. She also had multiple milia on the forehead, cheeks, eyelids, chin, neck and backs of the hands.

Histological report (Dr. Whimster).—(1) The lesion on the eyelid : Basal-cell carcinoma of hair-follicle type. (2) The lesion on the nose : Moderately well-differentiated hair-follicle naevus (tricho-epithelioma).

During the last four years thirteen similar lesions have arisen on the face and neck. They were situated as follows : In October 1948 three lesions on the tip of the nose, right cheek and upper lip. In November 1948 an ulcerated lesion arose on the right side of the neck. In December 1948 four grouped lesions occurred on the left side of the forehead, one of which ulcerated, and an isolated lesion on the left cheek below the eyelid. In May 1949 a similar lesion on the right side of the upper lip. In November 1950 two further lesions, one on the angle of the jaw, and one on the left upper eyelid. All these have been treated with x-rays with a good cosmetic result.

Present state.—In the last few weeks a number of new nodules have appeared in the right nasolabial fold and on the left side of the chin.

Comment.—This case is similar to three described in 1933 by Norman Paul as "Multiple naevoid rodent ulcers of the face."

The conditions occurs in adults, and multiple lesions of varying size are distributed over the face, neck and ears. There is no special localization ; new lesions appear from time to time, which ulcerate early and become destructive.

The lesions begin as small pearly nodules, which later umbilicate and break down in the centre. They occur without keratoses or other sequelae of sunlight, and are associated with other naevoid lesions, such as milia.

The histological picture is a constant one. The basal-cell epitheliomata are of the hair-follicle or keratotic type, the cell masses being composed of elongated cells lying concentrically. At the edge of these masses immature hair follicles may be seen.

Paul separates this type of case from epithelioma adenoides cysticum for the

following reasons: In Brooke's disease there is often a family history, the onset is usually at puberty, the lesions are grouped and in the early stages symmetrical. They are also of uniform size and do not ulcerate.

This case exhibits lesions varying from organoid structures such as milia and trichoepitheliomata to frankly malignant basal-cell epitheliomata. The latter appear to be identical with Paul's "Multiple naevoid rodent ulcers of the face."

REFERENCE.

PAUL, NORMAN (1933) *Cutaneous Neoplasms*. Lewis.

Dr. C. H. WHITTLE: I suggest that the case belongs to the category of Brooke's tumours. Savatard (1938) described single as well as multiple lesions and some cases had no family history.

REFERENCES.

SAVATARD, L. (1938) *Brit. J. Derm.*, **50**, 333.

SUTTON, R. L., and SUTTON, R. L. (jun.) (1939) *Diseases of the Skin*. London: Henry Kimpton, p. 675.

The PRESIDENT: Those of us who went to Holland in the late summer will remember that Professor Zoon showed an identical case associated with Recklinghausen's disease.

The following cases also were shown:

Urticaria Pigmentosa in Brother and Sister. -Dr. D. S. WILKINSON.

Multiple Intraepidermal Epitheliomata (Bowen's Disease). -Dr. E. WADDINGTON.

CURRENT LITERATURE.

DERMATITIS AFTER USE OF PENTAVALENT ARSENICALS PER VAGINAM. W. E. Orchard. (1951) *Brit. med. J.*, **2**, 1444.

Pentavalent arsenicals are commonly used as powders or pessaries to treat trichomonal vaginitis and also for symptomatic treatment of non-specific leucorrhoea. A woman aged 21 who had formerly suffered from a generalized exfoliative dermatitis following 7 injections of arsphenamine diglucoside subsequently developed a generalized dermatitis, thought to have been due to the use of Stovarsol vaginal compound pessaries in the treatment of leucorrhoea. Reference is made to a reported case in which intolerance to trivalent arsenic was subsequently followed by sensitivity to the pentavalent form. B. A. T.

IMPETIGO HERPETIFORMIS. L. E. Pierini and L. C. Mendivil. (1951) *Rev. argent. dermatosif.*, **35**, 19.

Very shortly after subtotal thyroidectomy 19 years earlier a non-pregnant woman, now aged 45, developed severe hypoparathyroidism, for which she did not continue adequate regular treatment and later developed cataract. After 11 years she developed an extensive erythrodermia similar to her present attack, in which the essential lesions of impetigo herpetiformis were identified both clinically and histologically. Exhibition of dihydrotachysterol cleared her skin and raised her blood calcium level to normal. The undoubted connection here of parathyroid disturbances with impetigo herpetiformis supports previous hypotheses on the pathogenesis of this skin affection. G. W. B.

ADENYLIC ACID IN THE TREATMENT OF PRURITUS. M. I. Quiroga, C. F. Guillot, A. Parodi and R. N. Corti. (1951) *Rev. argent. dermatosif.*, **35**, 29.

A report that adenylic acid, a phosphomononucleotide, relieved pruritus in some cases of Hodgkin's disease led the authors to investigate its antipruritic action. On three consecutive days 20 mg. sodium adenosin-5-monophosphate was injected intramuscularly hourly for 5 hours into 10 patients, of whom 6 were considerably relieved, 2 were perhaps improved and 2 were uninfluenced. The acid has a fundamental importance in the intermediate metabolism of carbohydrate. As a working hypothesis the authors suggest that in pruritus the enzyme adenosinetriphosphatase is inhibited by an excess of histamine. Activators of this enzyme are adrenalin and the ions of Mg, Ca and Co, particularly the Mg ion. Experimentally the lower the concentration of Mg ions the greater the inhibition of the enzyme by histamine. G. W. B.

ACTH AND CORTISONE IN DISEASES OF THE SKIN. W. F. Lever. (1951) *New Engl. J. Med.*, **245**, 359.

The effect of ACTH or cortisone on more than 70 patients with diseases of the skin is described. Results were excellent in pemphigus (all varieties), systemic L.E., dermatomyositis and idiopathic generalized exfoliative dermatitis. Psoriasis, dermatitis herpetiformis, sarcoidosis, atopic eczema and scleroderma benefited temporarily. A case of mycosis fungoides improved slightly after two courses of treatment.

The usual dose was 25–50 mg. six-hourly of ACTH intramuscularly. A. D. P.

ENDOGENOUS OCHRONOSIS. H. Friderich and W. Nikolowski. (1951) *Arch. Derm. Syph., Berl.*, **192**, 273.

The abnormal pigment in ochronosis is difficult to demonstrate in affected skin, though readily in cartilage. A patient, however, had three naevi which clinically resembled blue naevi, but which, on histological examination, proved to be cellular naevi in which the special pigment was deposited and readily demonstrated in the sections. M. F.

SPOROTRICHOSIS OF THE GENITALIA. H. Weichardt. (1951) *Arch. Derm. Syph., Berl.*, **192**, 290.

After incision of a periurethral abscess a fistula remained and would not heal in spite of penicillin. The right bulbus cavernosus became thickened, the skin over it red; the right testicle

swelled, then the vas deferens thickened and the inguinal glands enlarged: finally both epididymes were involved. A biopsy in the region of the fistulous opening showed many Russell's bodies.

Mycological findings, and the results of guinea-pig, rat and mice inoculations which confirmed sporotrichosis, are given in detail. M. F.

CHANGES IN CUTICLE OF HUMAN HAIR AFTER IRRADIATION AND USE OF HAIR LOTIONS. H. C. Friederich. (1951) *Arch. Derm. Syph., Berl.*, **192**, 310.

Sunlight and ultra-violet light damaged the cuticle, as was demonstrated in photo-micrographs. Hair lotion did not appear to be harmful unless used for a lengthy period. When sunlight is employed therapeutically, the hair should be carefully parted to expose the scalp. M. F.

INHERITANCE OF VASCULAR NAEVI. G. Tiedemann. (1951) *Arch. Derm. Syph., Berl.*, **192**, 327.

The author concludes that his findings point to inheritance. Family trees, studies of twins, association with other congenital defects point to a "dihybrid-recessive inheritance with partial sex-linkage on the assumption of an 'anlage-pair,' one specifically pathological and the other physiological." M. F.

STUDIES OF MESENCHYMAL FORMATIONS IN BASALIOMAS. H. Reich. (1951) *Arch. Derm. Syph., Berl.*, **192**, 382.

Miescher noted granulomatous formations composed of small, polymorphous histiocytes, often radially arranged in erythema nodosum and in the nodose eruption produced by sulphonamides. Now Reich reports similar structures in the region of cutis and subcutis in basalioma. M. F.

IS MYCOSIS FUNGOIDES A RETICULO-ENDOTHELIAL NEOPLASTIC ENTITY? Edward P. Cawley, Arthur C. Curtis and James E. K. Leach. (1951) *Arch. Derm. Syph., Chicago*, **64**, 255.

The authors review 10 cases clinically typical of mycosis fungoides. Autopsy showed involvement elsewhere in 8 cases. Pathological diagnosis of Hodgkin's disease was made in 3 cases, of lymphoblastoma of reticulo-endothelial-cell type in 3, of lymphoblastoma with a preponderance of lymphoblasts but not typically lymphosarcoma or leucaemia in 3, and mycosis fungoides with characteristic polymorphous cutaneous infiltration in 1. They conclude that mycosis fungoides is classifiable among the lymphoblastomas, and that it is a clinical but not a pathological entity. J. K.

CLINICAL STUDIES IN PERCUTANEOUS ABSORPTION. M. V. Nadkarni, Donald B. Meyers, Robert G. Carney and Louis C. Zopf. (1951) *Arch. Derm. Syph., Chicago*, **64**, 294.

The authors found greater absorption of an insoluble dye by the normal skin when using a water-soluble vehicle than with an oily base. Absorption was more rapid and in greater quantity in persons aged 35 to 64 than in older or younger subjects. The male skin absorbs better than the female and the inflamed skin than the normal. Further study is being undertaken. J. K.

SUCCESSFUL TREATMENT OF PEMPHIGUS WITH HEPARIN. John P. Magner, R. Campbell Manson and Allen Pepple. (1951) *Arch. Derm. Syph., Chicago*, **64**, 320.

After 5 months in hospital without improvement a patient suffering from pemphigus was given 200 mg. daily of delayed absorption type heparin. Within 4 days the lesions had disappeared and two months later he was still clear. *O! Si sic omnes!* J. K.

PSYCHOCUTANEOUS ASPECTS OF PERSISTENT PRURITUS AND EXCESSIVE EXCORIATION. Philip F. Durham Seitz. (1951) *Arch. Derm. Syph., Chicago*, **64**, 136.

This condition arising from a masochistic tendency in the patient is characteristically associated with suppressed feelings of anger and resentment. There is a danger that during a permissive psychotherapeutic approach on the part of the physician "explosive reactions of aggressive rage are precipitated by the interviews." If such reaction does not occur in presence of the physician, he being too permissive, the patient may act out his hostility at home or elsewhere. This, as the author truly states, is frequently worse than the disease, and must be avoided by "skilfully controlled relationship between the patient and his physician." J. K.

EFFECTS OF PODOPHYLLUM ON BASAL-CELL EPITHELIOMAS. Charles F. Sims and Nathan Pensky. (1951) *Arch. Derm. Syph., Chicago*, **64**, 142.

An unsuccessful attempt to treat 20 basal-cell epitheliomas with 25% podophyllum resin in alcohol or liquid paraffin for from 2 to 7 days. No regression or cure was observed in any epithelioma. J. K.

PYOGENIC INFECTIONS OF SKIN: ETIOLOGIC FACTOR IN ACUTE GLOMERULONEPHRITIS OF CHILDREN. J. Lamar Callaway and Harry B. O'Rear. (1951) *Arch. Derm. Syph., Chicago*, **64**, 159.

Although upper respiratory infections are regarded as the principal causes of nephritis in children, 36 of 76 patients had not had such an infection but had had a preceding superficial pyodermia. Mercury used to treat the skin affection was not a causal factor in producing the nephritis. J. K.

TREATMENT OF VESICULO-EROSIVE STOMATITIS WITH AUREOMYCIN TROCHES. Alexander A. Fisher and Morris Leider. (1951) *Arch. Derm. Syph., Chicago*, **64**, 164.

Troches each containing 15 mg. aureomycin were used to treat 8 cases of vesiculo-erosive stomatitis with benefit to 6 patients, 2 of whom had to continue the treatment indefinitely to maintain freedom from symptoms. One patient developed mild diarrhoea and two pruritus ani: these conditions disappeared spontaneously. In 2 patients a new generalized stomatitis appeared; 1 discontinued treatment, the other was benefited by the simultaneous administration of riboflavin. J. K.

PIGMENTED PURPURIC ERUPTIONS. Samuel J. Randall, Robert R. Kierland and Hamilton Montgomery. (1951) *Arch. Derm. Syph., Chicago*, **64**, 177.

The authors, reviewing 72 cases of Schamberg's disease, 12 of angioma serpiginosum, 4 of pigmented purpuric lichenoid dermatitis of Gougerot and Blum and 4 of purpura annularis telangiectodes seen at the Mayo Clinic during the past 30 years, conclude that the first 3 are closely related if not merely cutaneous expressions of a single process in different degrees. Purpura annularis telangiectodes may be a morphological entity, but this question requires study of a larger number of cases. J. K.

ALLERGY TO PITUITARY CORTICO-TROPHIC HORMONE. S. M. Feinberg, A. R. Feinberg and E. Bigg. (1951) *J. Amer. med. Ass.*, **147**, 40.

A patient with rheumatoid arthritis who had received ACTH the previous year developed a severe allergic reaction, and was found to be allergic to all forms of corticotrophin in high dilution and to other pituitary preparations. A. J. R.

DECUBITUS ULCER IN RHEUMATIC FEVER TREATED WITH CORTISONE. J. G. Barrow and C. R. Sikes. (1951) *J. Amer. med. Ass.*, **147**, 41.

A girl aged 13, receiving cortisone for rheumatic fever, developed a sacral decubitus ulcer which failed to heal. It is assumed that cortisone suppressed the normal mechanism of wound healing, and it is suggested that if this complication develops the cortisone should be stopped. A. J. R.

THROMBOCYTOPENIC PURPURA IN PREGNANCY. L. J. Glick and N. J. Weiser. (1951) *J. Amer. med. Ass.*, **147**, 44.

A negro woman aged 24 had thrombocytopenic purpura which failed to respond to splenectomy in pregnancy. Failure is attributed to an accessory spleen, but a post-mortem examination was not permitted. In thrombocytopenic purpura the indications for splenectomy should be considered without reference to pregnancy. A. J. R.

PODOPHYLLUM RESIN IN TREATMENT OF TINEA CAPITIS. F. Reiss and D. D. Doherty. (1951) *J. Amer. med. Ass.*, **147**, 225.

One hundred and twenty-one cases of tinea capitis were treated with 0·2% podophyllum resin in an aquaphor or carbowax base. Although the results do not appear to be significantly better

than those obtained with other local applications, the authors suggest that the treatment may be useful, particularly when further treatment is necessary after x-ray epilation.

A. J. R.

SARCOIDOSIS BENEFITED BY PREGNANCY. R. H. Berman. (1951) *J. Amer. med. Ass.*, **147**, 246.

The literature on pregnancy in sarcoidosis is briefly reviewed, and a case is reported in which two normal full term pregnancies apparently each produced improvement in the sarcoidosis.

A. J. R.

DRUG FATALITIES. N. Flaxman. (1951) *J. Amer. med. Ass.*, **147**, 377.

Since December, 1946, 107 drug fatalities have been reported in the literature (presumably that of the United States, but this is not stated). Cases of accidental or suicidal poisoning are excluded. Of special interest to dermatologists are the 6 deaths due to penicillin from exfoliative dermatitis, Herxheimer reactions or anaphylactic shock, and the 5 deaths from streptomycin as a result of toxic encephalopathy, dermatitis and stomatitis. The need for continued caution when the sulphonamides are prescribed is emphasized. The author suggests that as thiocyanates and cinchophen are of questionable value and regularly cause severe toxic effects or death they might be withdrawn from the market. A. J. R.

HAIR LOSS AND PIGMENTATION DUE TO THIOURACIL DERIVATIVES. M. Wilburne. (1951) *J. Amer. med. Ass.*, **147**, 379.

The side effects previously reported are summarized. The case is reported of a woman aged 67 with hyperthyroid heart disease. Both methylthiouracil and propylthiouracil produced pronounced hair loss and yellowish pigmentation of the previously white hair. A. J. R.

ERYTHEMA MULTIFORME EXUDATIVUM. V. S. Wammock, A. A. Bierderman and R. S. Jordan. (1951) *J. Amer. med. Ass.*, **147**, 637.

A man aged 23 with Stevens-Johnson syndrome was treated with ACTH. There was a dramatic symptomatic response, and healing of the lesions was considered to be more rapid than in untreated cases. A. J. R.

OCCURRENCE OF SKIN PIGMENTATION DURING MESANTOIN THERAPY. H. Hunter and D. Jenkins. (1951) *J. Amer. med. Ass.*, **147**, 744.

A striking patchy brownish pigmentation somewhat resembling chloasma, affecting only the face and neck, developed in 6 patients with epilepsy who had been receiving mesantoin for more than a year. There were no other toxic manifestations. Careful investigation revealed no evidence of functional adrenal disturbance. The pigmentation gradually faded when the drug was stopped. A. J. R.

SYSTEMIC BLASTOMYCOSIS COMPLICATED WITH PREGNANCY. R. O. Noojin and H. B. Praytor. (1951) *J. Amer. med. Ass.*, **147**, 749.

A negro woman aged 21 was delivered of a normal infant 4½ months after developing signs and symptoms of systemic blastomycosis. The child has remained normal after a year. Passive transfer of complement-fixing antibodies from the mother was demonstrated immediately after birth. The antibodies disappeared from the infant's blood within 3 months. A. J. R.

SILICON GRANULOMA OF SKIN DUE TO TRAUMATIC SAND INOCULATION. J. E. Ginsberg and L. A. Becker. (1951) *J. Amer. med. Ass.*, **147**, 751.

Extensive silicon granulomata developed after an interval of nearly 7 years at the site of perforating wounds contaminated with sand. The authors consider that oral and local aureomycin may have contributed to the regression of the granulomata as this rarely occurs spontaneously. A. J. R.

PAPILLOMA OF THE UMBILICUS. S. Vernon. (1951) *J. Amer. med. Ass.*, **147**, 755.

A report of a case which the author claims to be only the fifteenth in the literature. The patient was a girl aged 13 and the lesion had been present for 3 weeks. The clinical and histological problems presented in differential diagnosis are discussed. A. J. R.

THE INDUSTRIAL HEALTH MOVEMENT WITH SPECIAL REFERENCE TO DERMATOSES. J. E. Dalton. (1951) *J. Amer. med. Ass.*, **147**, 799.

A long and interesting survey of the development of industrial health activities in the U.S.A. is followed by a brief account of the industrial dermatitis problem. Industrial skin disease in the United States costs one hundred million dollars a year (one hundred dollars per case). Other statistics emphasizing the importance of industrial skin disease are given. A. J. R.

PREPUBERTAL MALIGNANT MELANOMA. R. J. Coffey and W. T. Berkeley. (1951) *J. Amer. med. Ass.*, **147**, 846.

Malignant melanoma before puberty is very rare. Although certain histological features may suggest malignancy the clinical course usually fails to support this. The 3 reported cases of demonstrable metastasis from prepubertal melanomas are reviewed. A new case is reported of a melanoma in a girl aged 7 with metastasis to the left inguinal nodes. There was no recurrence 2 years after surgical treatment. Histologically the melanoma was of the sarcomatous type without activity at the dermo-epidermal junction. A. J. R.

ACUTE LUPUS ERYTHEMATOSUS WITH RETICULOSIS AND WITH PARTICIPATION OF RETICULUM CELLS IN THE FORMATION OF L.E. CELLS. H. Hauser. (1951) *Derm. Wschr.*, **124**, 906.

A patient with acute lupus erythematosus, nephritis, retinal changes and leukopenia, with L.E. cells in marrow and peripheral blood suddenly developed a reticulosis with flooding of the peripheral blood with reticulum cells not normally found there. The author finds that not only neutrophil leucocytes can form L.E. cells but eosinophils also, and reticulum cells as in this case. Microphotographs illustrate the test. M. S. S.

LOCALIZED ICHTHYOSIS VULGARIS. H. Hermann. (1951) *Derm. Wschr.*, **124**, 1097.

In the author's opinion ichthyosis of the palms and soles is not infrequently confused with congenital keratoderma of the palms and soles, but ichthyosis is essentially drier from the relative absence of sweat glands, and it lacks on the palms and soles the sharp demarcation and red border of congenital keratoderma. He gives the family history of a girl aged 9 with generalized ichthyosis, whose palms and soles were normal but whose nails were hard and brittle. The mother, grandmother and three grand-aunts had all abnormally thick dry skin on the palms and soles and deformed nails, but sound skin otherwise. The great-grandfather and great- great-grandfather appear to have had generalized ichthyosis and abnormal finger-nails. The dystrophy of the palms, soles and nails in this family the author regards as localized ichthyosis.

M. S. S.

THE TREATMENT OF CHRONIC URTICARIA. H. Stuhlert. (1951) *Derm. Wschr.*, **124**, 909.

The author has had success in treating otherwise intractable chronic urticaria with cardiazol and a stable solution (Causat, prepared by Reiss, Berlin) containing novocaine 0·1 g., acid phenylethylbarb. 0·025 g. and atropine sulph. 0·0003 g. After three days of cardiazol 0·2 g. by mouth every three hours from 7 a.m. to 10 p.m., on the fourth day 6 ml. of the novocaine solution were given intravenously, the next day 8 ml. and the next 10 ml.: this dose was not exceeded, but was repeated daily for seven more days. The treatment was found to be more effective when focal sepsis and other contributory factors were dealt with first. In all nine cases were treated, as in-patients. Most had a recurrence of some degree following the course, but the majority were much benefited. There were two failures. M. S. S.

THE ACTION MECHANISM OF CHRYSAROBIN. P. Nánási and A. Kocsis. (1951) *Derm. Wschr.*, **124**, 1001.

The authors seek to find whether chrysarobin owes its activity to OH phenol groups, as is held, or to its reducing capacity. To find if the quinone compound in chrysarobin is the active reducing agent they tested the therapeutic activity of the phenol groups in cyclical compounds with one ring (resorcin and hydroquinone), two rings (α and β naphthol), and three rings (anthracene and anthraquinone). Resorcin had an effect and hydroquinone a better, but neither so good as chrysarobin; α and β naphthol had about the same effect as chrysarobin, the former accompanied by epidermal destruction and pigmentation, the latter not. Anthracene and anthraquinone were without result. To test more particularly the action of the combined quinone

derivatives against the OH phenolic groups alizarin and alizarin sulpho acid sodium were used. Both had an action, the latter more marked, owing probably to the increase of solubility in water due to the sodium sulphate radical. Sulphonating chrysarobin to increase its solubility diminished its activity. That the antipsoriatic action of chrysarobin disappears when it is oxidized to chrysophanic acid the authors feel to be due to the latter's being really a peroxidized disintegration product. They tried the effect of oxidizing chrysarobin so as to leave the OH phenol groups unaltered. The product had some action, but not nearly so pronounced as chrysarobin.

The authors conclude that in the therapeutic activity of chrysarobin both the OH phenolic groups and reducing power take part. M. S. S.

ACTION OF HYALURONIDASE ON FOREIGN BODY GRANULOMA. G. Polemann. (1951) *Derm. Wschr.*, **124**, 1029.

The author, by treating a foreign body granuloma in the mouse with hyaluronidase, seeks to find if the connective-tissue encapsulation of the foreign body is reversible. He describes in detail his experiments on 46 mice. There was no important difference in the foreign body granulomas treated with hyaluronidase and an equal number left untreated. M. S. S.

THE THERAPEUTIC USE OF HYALURONIDASE. M. Schoog. (1951) *Derm. Wschr.*, **124** 1033.

The author discusses the chemistry and physiology of hyaluronic acid and chondroitin sulphuric acid and describes the action of hyaluronidase, pointing out that this may vary according to the source, e.g., that obtained from the testis can act on both acids, whereas hyaluronidase obtained from streptococci can act only on hyaluronic acid. The strength of action of hyaluronidase depends also on the pH, temperature and salt concentration of the surroundings and the presence of activators or inhibitors.

The author used Kinetin (Schering) as his source of hyaluronidase to treat five patients with scleroderma, circumscribed and diffuse, one injection daily or on alternate days intra- or subcutaneously of an ampoule containing 10 Schering units, with no other therapy in order to avoid a possible inhibiting action. No therapeutic effect was obtained. This is in keeping with the fact that cortisone which benefits scleroderma is a hyaluronidase inhibitor. Also ineffective in the author's experience was the use of penicillin hyaluronidase locally in chronic recurring erysipelas, or the injection of hyaluronidase with impletol or an anti-histamin in genital or anal pruritus. M. S. S.

ARTHUS PHENOMENON AFTER INTRA-EPIDERMAL HYALURONIDASE WHEAL. H. Wohnlich. (1951). *Derm. Wschr.*, **124**, 1124.

In a patient with phthisis who had a gland operation scar at the angle of the jaw an intradermal injection of hyaluronidase produced an Arthus phenomenon actually during the injection, with acute anaemia at the injection site followed immediately by livid discoloration and shrinking of the area. Wheals produced immediately after below the site showed a distinctly smaller reaction or none at all, indicating a kind of immunity reaction following the first injection. A control wheal with saline gave no reaction. Injection wheals with Hibernon developed practically without complication, and there was no evidence of an inhibited spreading effect as in normal patients.

In a second patient showing an Arthus phenomenon (for the first time after a sixth injection) the necrosis was not so great, but as in the first patient the reaction to subsequent injections became progressively less. A Prausnitz-Küstner test with the patient's serum caused extensive necrosis and death of a guinea-pig in twelve hours. With ordinary serum the reaction to hyaluronidase was smaller, but more than in a control with no prior injection. Both these guinea-pigs lived after the test. M. S. S.

TREATMENT OF BISMUTH STOMATITIS WITH SULFACTIN (BAL). W. Schmidt. (1951) *Derm. Wschr.*, **124**, 1121.

The author treated 5 cases of bismuth ulceration of the oral mucous membrane, accompanied by haematuria and in some instances pyrexia, with sulfactin (BAL). The results were uniformly excellent, with healing of ulceration and disappearance of haematuria in four, six or ten days according to severity. The dosage for the most part was 2 ml. intramuscularly two to four times daily for the first three or four days and finally one injection daily till well. There were no side-effects apart from pain at the site of the injection in one patient. M. S. S.

APPENDIX TO THE PRECEDING WORK OF W. SCHMIDT: TREATMENT OF BISMUTH STOMATITIS WITH SULFACTIN (BAL). H. Löhe. (1951) *Derm. Wschr.*, **124**, 1124.

The author is able to endorse the excellent results obtained by Schmidt with the use of BAL in bismuth stomatitis. He himself has had equally satisfactory results in salvarsan dermatitis, 4 cases of bismuth dermato-stomatitis and 3 of gold dermatitis, without side-effects. The subjective symptoms vanish astonishingly with the first two or three injections, and the objective signs in skin, renal system, etc., follow after a further series of injections. M. S. S.

TREATMENT OF PSORIASIS PATCHES WITH RESPIRATORY STIMULATING AND INHIBITORY MEANS. A. Kocsis and P. Nánási. (1951) *Derm. Wschr.*, **124**, 1003.

The authors discuss the findings of those who have investigated the intracellular respiration of the skin. Normal cornification depends on various amino-acids, and in particular on sulphur-containing amino-acids. In an attempt to diminish the activity of these acids in psoriasis the authors introduced various heavy metal ions into the skin by electrophoresis. Ferric and permanganate ions healed the psoriasis patches (only fresh nummular ones, not old ones); ferrous, cuprous, cupric, mercurous, plumbic and cobaltic ions had a flattening effect without healing. Cobaltous and mercuric ions caused necrosis, without healing. Arsenic, resorcin, pyrogallous acid and ascorbic acid had no result, but hydroquinone was effective. The therapeutic activity of the ferric and permanganate ions and hydroquinone apparently depended on the stimulation of intracellular respiration (chrysarobin possesses a quinone structure). As cyanogen specifically inhibits respiration the authors now introduced this by iontophoresis or injection using calcium cyanide; they used also the inhibitor malonic acid without result on the psoriasis. Narcotics, such as ether urethane and chlorethyl, were also used without result. As the normal ferment activity and oxidative processes necessary for pigment formation are held to be disturbed in psoriasis the authors injected novocaine, reported to promote oxidation, but this produced no result, nor did tyrosin. M. S. S.

SKIN CANCER. P. Childs. (1950) *Med. Pr.*, **224**, 506.

In 1945, more than 600 men and 500 women died from cancer of the skin: the author maintains that many of these deaths should not have occurred. To prevent this, all tumours of the skin should be regarded as being malignant until proved otherwise.

Precancerous lesions such as senile keratoses and areas of leukoplakia should be treated and watched carefully for malignant change. With established epitheliomata, the guiding principle of treatment, no matter what method is used, is that it must be adequate. Complete excision is the author's preference, but in many cases best results are obtained by the surgeon and radiotherapist working together.

All pigmented moles that are exposed to mechanical trauma should be excised completely. If malignant change occurs, wide excision offers the only hope of cure and that hope is very slender. H. R. V.

THE RELATIONSHIP BETWEEN HERPES ZOSTER AND VARICELLA. C. H. Barnett. (1950) *Med. Pr.*, 223, 126.

The objections to the theory that varicella and herpes zoster are caused by the same virus are presented in detail, and cases are given illustrating the various points. The theory is advanced that the clinical picture produced by the virus depends on the state of immunity of the host: when this is low, varicella is produced, when moderate, herpes zoster, and when high, there is subclinical infection. Following this, the virus may remain latent for many years, sometimes being reactivated by trauma to the posterior root ganglion. H. R. V.

MODERN TRENDS IN THE TREATMENT OF ACNE AND SEBORRHOEA. F. Glyn-Hughes. (1950) *Med. Pr.*, 223, 309.

The seborrhoeic eruptions, rosacea, acne vulgaris, pityriasis capitis and corporis, seborrhoeic dermatitis and eczema are different manifestations of the same underlying process, the appearance being dependent upon certain factors such as age, diet, mode of life, emotional state and secondary infection.

In treating these conditions, internal treatment, either by drugs or hormones, reinforced by regulation of diet, mode of life and emotional experience, is of prime importance. These points are elaborated, and local treatment following generally accepted lines is considered in detail. H. R. V.

COMMON SKIN DISEASES IN CHILDREN. E. Colin Jones. (1950) *Med. Pr.*, 224, 450.

This article outlines the treatment of impetigo, eczema, papular urticaria and warts in children. Generally accepted methods are used, and for impetigo, local penicillin is given as the method of choice.

Papular urticaria is stated to be " undoubtedly dietary in origin " and charming is advocated in the treatment of warts, though whether thorium X acts as a charm or by its radioactivity is not stated. H. R. V.

MODERN TREATMENT OF PSORIASIS. J. T. Ingram. (1950) *Med. Pr.*, 224, 5.

This excellent article should be read by all interested in this condition. Particular stress is given to the importance of making the unfortunate patient realize that something active can be done for him even though the improvement may not necessarily be lasting.

The main attack is daily baths—to which liq. picis carb. 4 oz. to 30 gallons may be added—general U.V.R. and local application of Lassar's paste incorporating dithranol in strength $\frac{1}{2}$ to 2 grains to the ounce.

Dermatological departments in hospitals should be equipped to deal adequately with psoriasis both for active treatment and for after-care. H. R. V.

THE VALUE OF VITAMINS IN THE TREATMENT OF SKIN DISEASES. A. G. Smith. (1951) *Med. Pr.*, 226, 401.

In dermatology vitamins are useful in two groups of conditions, those in which the skin lesion suggests a definite deficiency, and those not necessarily associated directly with a deficiency but which are relieved or cured with certain vitamins.

The different vitamins are considered alphabetically. In addition to classical vitamin A deficiency, characterized by phrynoderma, this vitamin in large doses may also benefit other dermatoses showing dyskeratosis—xeroderma and ichthyosis, keratosis pilaris, Darier's disease and pityriasis rubra pilaris. Vitamin B may help herpes zoster, lichen planus and pink disease. Classical B_2 deficiency is characterized by cracking and exfoliation of the lips, fissuring at the angles of the mouth, a painful, purplish tongue, an eruption of erythematous greasy plaques in the naso-labial folds and scrotal dermatitis; lack of nicotinic acid is mainly responsible for pellagra, and the author uses this substance in conjunction with local therapy to treat chilblains and erythrocyanosis crurum. Vitamin C lack appears as scurvy, and this vitamin also hastens the cure of leg ulcers and dermatitis due to sulphonamide, arsenic and gold. The treatment of lupus vulgaris with vitamin D is given in detail, and its use in other tuberculous manifestations of the skin and sarcoidosis is mentioned. Vitamin E may help in granuloma annulare, lupus erythematosus and the type of alopecia seen in menopausal women. In concluding the list, vitamin K may help cases of spontaneous haemorrhage of the newborn and certain cases of purpura. H. R. V.

MODERN TRENDS IN THE TREATMENT OF SKIN DISEASES. W. P. Elford and R. Varley. (1950) *Med. Pr.*, 223, 246.

In this comprehensive review of the newest methods of dermatological therapy the authors stress that success in treatment depends largely on accurate diagnosis and knowing what to avoid in any particular case.

The role of the endocrine glands particularly in regulating sebaceous activity and pigmentation is described. Of the vitamins, D_2 for lupus vulgaris and A for Darier's disease and pityriasis rubra pilaris are particularly mentioned, and vitamin E may play a part in collagen disease. Local application of sulphonamide should be avoided, and if penicillin is used, a sterile watery solution is preferable. Since tyrothricin cannot be given systemically, it has a place in local therapy.

Many new effective fungicides have been introduced, but epilation is still the only effective method of treating scalps infected with *M. audouini*.

The use of BAL for dermatitis produced by the heavy metals and the treatment of neoplasms by local application are mentioned. H. R. V.

THE EFFECT OF CORTISONE THERAPY ON BREAST CARCINOMA METASTASIZING TO THE SKIN. Harold C. Fishman. (1951) *Urol. and cutan. Rev.*, 55, 319.

It did not influence the growth, but entirely relieved the pruritus associated with radio-dermatitis. C. H. W.

"L.E." CELL PHENOMENON AND IN VITRO CORTISONE. Theodore Cornbleet and Francis T. Flood. (1951) *Urol. and cutan. Rev.*, **55**, 208.

Cortisone added to "L.E." serum (5 cases) plus normal dog bone marrow did not inhibit the formation of "L.E." cells. C. H. W.

A CONCEPT OF ALLERGY (FROM A VIEWPOINT OF A DERMATOLOGIST). Max Popper. (1951) *Urol. and cutan. Rev.*, **55**, 301.

A thoughtful review of a difficult subject. Conclusions: Allergy may be a physiological asymptomatic normal and universal process. Symptomatic or pathological, allergy may be a dysfunction of the antibody-producing mechanism. Two different kinds of antibody may be produced by the same antigen, the union of one type with the antigen yielding no ill-effects, the other type in uniting with the antigen giving rise to allergic disease. The importance of heredity in conditioning the reaction is stressed. C. H. W.

THORIUM-X INVESTIGATIONS: HISTOLOGICAL STUDY OF THORIUM-X APPLICATION ON RABBIT SKIN. H. C. Fishman. (1950) *J. invest. Derm.*, **15**, 71.

Only since the war has thorium-X been easily obtainable in the U.S.A. and, possibly because of a more widespread knowledge of radioactivity, its therapeutic action has been exploited with greater caution than in Europe. The present study is concerned only with epidermal changes, the unfamiliar structure of the rabbit's dermis making practically insuperable the well-known difficulties of assessing changes in that tissue.

Vacuolization of the prickle cells is followed by hyperkeratosis. Degrees of change are graded by the author as "very marked," "definitely marked," "marked" and "much less marked." J. H. T. D.

CUTANEOUS SARCOIDOSIS AS AN EXPRESSION OF SYPHILIS: REPORT AND DISCUSSION OF A CASE. E. T. Bernstein and M. Leider. (1950) *J. invest. Derm.*, **15**, 75.

The histological structure of the lesion in this case of late syphilis was indistinguishable from that of Boeck's sarcoid. Tuberculin (O.T.) reaction was positive 1 : 1,000,000, and diagnostic B.C.G. vaccination produced "normergic" response. The conclusion is drawn that sarcoidosis may sometimes be no more than the reaction to syphilitic, leprous or tuberculous infection in one who has developed an unusual type of immunity. At least that is presumably the meaning of "in our view they are the run of the mill cases one sees hereabout." J. H. T. D.

THE RELATIONSHIP OF HOST AND VIRUS IN MOLLUSCUM CONTAGIOSUM. G. Rake and H. Blank. (1950) *J. invest. Derm.*, **15**, 81.

This paper contains (i) a histochemical study of the maturation of the epidermal cell into a molluscum body, and (ii) an electron-microscope examination of the virus itself in relation to the debris of the cell which has harboured it. The considerations adumbrated in the title are not discussed.

The authors first describe the molluscum inclusion body as "a minute ovoid structure within the cytoplasm of the basal cell, which as it grows distorts the cell to produce the condition known as dyskeratosis." Then they show by the Feulgen method of staining with basic fuchsin that the first change is an increase of ribonucleic acid in the cytoplasm. The next change is an appearance of islands of desoxyribonucleic acid (presumed to correspond with the substance of the virus itself), which enlarge to distend the existing ribonucleic acid matrix into a sponge- or net-like structure. A similar pattern can be discerned in sections stained with Unna-Pappenheim. The electron micrographs show the brick-shaped virus particles that have already been demonstrated in the supernatant fluid after centrifuging an emulsion of material squeezed from lesions. But ignoring what they call the supernates (nothing to do with Hottentot anatomy), they have studied mainly the centrifuge deposit. The photographs show the virus particles as it were in process of crystallizing from an amorphous mass of smaller granules of approximately the same shape. Certain ringed fibres strongly resembling collagen fibrils are thought possibly to be part of the ribonucleic acid reticulum. J. H. T. D.